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ASPECTS OF ANÆSTHESIA*

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THOSE OF US whose professional experience extends back over several decades remember with considerable anguish personal adventures with chloroform, ether, or a mixture of the two. Oftentimes it was just as bad for one's peace of mind to be the administrator as the recipient of an anæsthetic. I would hate to have to re-enact the battles I have had with patients who did not appreciate the way they were being smothered. What a difference today! We do not give a straight ether induction often enough even to provide teaching experience for our students. Some may complain that the gases and intravenous barbiturates have wiped out all the art in the induction of anæsthesia, but I am sure the patients do not share that view. To know that one may go to sleep rapidly and pleasantly without any sense of suffocation is certainly a major improvement in anæsthesia because such knowledge banishes fear.

In enumeration of the principal changes in anæsthesia practice during the past decade I shall list the following items, each of which I propose briefly to discuss:

(1) Rational use of intravenous anæsthetics. (2) Introduction of curare and other muscle relaxants. (3) Increased appreciation of the value of gas anæsthetics, particularly nitrous oxide. (4) The recurrent spinal anæsthesia versus general anæsthesia controversy. (5) Better obstetrical anæsthesia. (6) Better training for anæsthetists, and the outlook for the future.

Pentothal, evipal, kemithal and surital are short-acting barbituric acid derivatives of slightly different chemical composition, which are used for intravenous anæsthesia. They are all comparatively safe and efficient when used properly, and may be extremely dangerous when used carelessly or when an attempt is made to use them for unsuitable purposes. Ether's reputation as the "safest" of all anæsthetic agents is based entirely on the fact that in ordinary doses it does not depress respiration. Whatever else patients may do, or attempt to do, under ether, they do not stop breathing except for an occasional transitory bout of breath-holding during induction. On the contrary, with intravenous barbiturates the first thing that happens after unconsciousness is respiratory depression, particularly when there is any tendency toward obstruction in the air passages. Since the cardinal principle of safe anæsthesia is adequate oxygenation through unobstructed airways, every doctor who administers an intravenous barbiturate should be equipped with the knowledge and the apparatus which may be necessary for artificial maintenance of respiration. Because of this potential danger there is no such thing as a "minor anæsthetic" with pentothal, even though the operation for which it is being given may be a very short one.

The barbiturates are not good analgesics and therefore are not suitable anæsthetic agents for long painful procedures, but they are ideal for short operations such as the reduction of dislocations, the incision of an abscess, or the removal of one or two teeth: and they are often ideal agents to use for induction only in longer operations. The qualified hospital anæsthetist, with his oxygen bags and masks, his endotracheal tubes and laryngoscopes does not fear respiratory arrest because it is easy for him to control it. He may therefore use intravenous barbiturates in situations which would be foolhardy practice for a general practitioner in his office or in a patient's home.

Another development in anæsthesia which has revolutionized hospital practice is the introduction of curare for muscle relaxation. But just because curare makes anæsthesia seem so easy, it

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may be for the patient an increased hazard. Curare, like the barbiturates is a respiratory depressant drug, and when the two are given together the patient often does not breathe spontaneously at all for half an hour or more. How important it is under such circumstances to know all about the safe control of respiration!

But I do not want to give the impression that curare is too dangerous for clinical use. It is now almost ten years since my colleagues and I had the temerity or the good fortune first to use curare for the relaxation of abdominal muscles in patients under anæsthesia. With awe and due humility we have seen it spread throughout the world, until now curare or some substitute relaxant is used in nearly every operating room. Accidents with it have happened, even under intelligent control, but I still marvel that such a potent drug can be so generally free of harmful consequences when one sticks to the rules. To be able to get good muscle relaxation with a rapidly acting, non-toxic controllable drug in combination with light anæsthesia is surely a blessing to surgeons as well as a boon to anæsthetists. Nowadays one does not hear nearly so much bad language in the operating rooms!

I am often asked my opinion regarding the relative safety or efficiency of the various curare preparations or curare substitutes which are now on the market. I wish it had been possible for us to become thoroughly familiar with all the aspects of d-tubocurarine before we were urged to try other relaxant drugs, each of which has its own special peculiarities. However, I suppose such a hope was vain in the case of a type of drug with such commercial possibilities. Now there is considerable confusion in regard to dosage between such preparations as syncurine, flaxedil, metubine, "Win 2747," mecostrin, decamethonium, etc., and claims and counter-claims regarding relative toxicity, degree of respiratory depression, etc.

My considered judgment at the present time about these drugs is that there is very little difference between them in clinical effectiveness, although there are slight differences in mechanism of their physiological action. The wise anæsthetist, particularly if he is only an occasional anæsthetist, should become familiar with one of these drugs, learn all about its dosage, its side effect, how to counteract overdosage, how to use it in combination with various anæsthetic agents, and not bother with any other relaxant. My personal predilection is still for d-tubocurarine chloride, although I am not denying the successful use of the other relaxants.

One result of the use of muscle relaxant drugs has been a new freedom of choice in anæsthetic agents. Nowadays with relaxation not a necessary concomitant of the anæsthetic drug, we have been able to explore more freely the possibilities of the gases, and to take advantage of their controllability and rapidity of action. This has led to a revival of interest in nitrous oxide for major surgery. Nitrous oxide is the least toxic and most rapidly eliminated of all anæsthetic agents, but quiet relaxed anæsthesia could be obtained with it only by the addition of ether or by dangerous deprivation of oxygen. Now, with curare, this gas can be used with plenty of oxygen even for thoracic and cardiac surgery, for small children and for the aged. All recent physiological and pathological studies tend to confirm the opinion that hypoxia can rapidly produce irreversible damage to the cells of the brain, liver, kidney and other vital organs. It is therefore the duty of the anæsthetist to administer his drugs with an adequate supply of oxygen, to make certain that this oxygen is freely delivered to the pulmonary alveoli, and to maintain the circulation in such a way that there may be a constant supply of oxygen to every body cell. This may now be done with nitrous oxide-oxygen when properly given, and also with ethylene-oxygen and cyclopropane-oxygen. Personally, I like cyclopropane and use it for a wide variety of surgical operations, but I do also admire and approve those who are reviving the skilful administration of nitrous oxide-oxygen.

In my own practice the advent of curare has had another curious and seemingly paradoxical result—an increase in the incidence of spinal anæsthesia. One may say, why use spinal technique when we have such other good relaxant drugs available? The only logical objection to spinal is the danger of complications, and my contention is that since we have curare to counteract an occasional failure to secure relaxation, we are able to use spinal anæsthesia techniques which are relatively safe. The safety factors include meticulously careful technique, the employment of *small* doses of dilute solutions of non-toxic drugs, injection by fine needles, and a careful selection of cases from both physical and psychological points of view.

Spinal anæsthesia has such a bad reputation

in bridge club gossip that I am sure there have been a great many bad spinal anæsthetics given. It should not be the method used by inexperienced anæsthetists, or be selected for patients "too sick for general anæsthesia," but I certainly believe it has an important place in modern anæsthesia. At the Homœopathic Hospital of Montreal during the past four years we have used spinal anæsthesia in 60% of our vaginal deliveries, and in most of our Cæsarean sections and hysterectomies. We pay careful attention to the safety factors I have outlined, and either for this reason or just by good luck we have had such freedom from bad results that both patients and surgeons are satisfied. I know that we cannot guarantee never to have a neurological complication, but neither can one guarantee always to avoid serious respiratory complications with ether, or cardiac complications with cyclopropane or chloroform. There is no *absolute* safety in anæsthesia.

Many patients say they do not want spinal anæsthesia when really what they mean to say is that they want to be asleep during the operation. We believe that it is actually better for most patients to be asleep during spinal anæsthesia; so rather than just "kidding" them, or lulling them with music, or "doping" them full of morphine, we let them go to sleep gradually and peacefully with an intravenous drip of 1:500 pentothal or light gas and oxygen. It is surprising what a small dose of spinal anæsthetic is needed when this combined "sleeping dose" technique is used. The only warning I want to emphasize is that in long cases one should beware of an overdose of pentothal. It is so easy to glide into barbiturate poisoning that we make an arbitrary limit of one gram as the maximum amount of pentothal permitted in any case. If more sleeping drug is needed one can always give one of the gases.

For maintenance of blood pressure and circulation during spinal or general anæsthesia our main reliance is on blood transfusions and fluid replacement, but occasionally a vasopressor drug may be needed for its temporary stimulating effect. I would like to say a word in recommendation of a new preparation—methoxamine ("Vasoxyl" B. & W.) which can be given to patients under cyclopropane without affecting the heart, and which produces a sustained peripheral vaso-constrictor effect without cerebral stimulation. Like all analeptic drugs it should be used only when definitely indicated and never as a routine.

Perhaps the most neglected field of anæsthesia is that of pain relief in obstetrics. In Canada today the vast majority of babies are born in hospitals, so I think we should try to set up methods of anæsthesia suitable for this situation rather than perpetuate routines which may be adequate for home deliveries. Whenever there is available a qualified anæsthetist, or even a doctor with reasonable skill in modern anæsthesia, I believe each woman in labour should have the benefit of his services. In our own hospital we have provided this type of specialist service routinely for the past five years, and both obstetricians and patients are highly enthusiastic about it. Patients do not object to paying a reasonable professional fee for services from which they have derived such obvious benefit.

I am not going to attempt here a description of all the techniques of obstetrical anæsthesia. I have stated that 60% of the deliveries in our hospital are done with spinal anæsthesia. The fact that this percentage has remained constant over a number of years is evidence that we do use individual judgment in deciding the method to be used for each particular case, and it is evidence also that this method for us gives continuing satisfaction. The situation in another hospital might be quite different. Choice of anæsthetic drug or method depends largely on the obstetrical routines which are generally followed. There is no doubt that spinal anæsthesia calls for a fairly high incidence of low forceps delivery. In our hospital the incidence of so-called "prophylactic" forceps was already high, so the introduction of spinal made no difference in this regard.

I believe that small-dose spinal anæsthesia, using the 1% procaine technique (advocated by Dr. R. J. Fraser of Hamilton) is safer, simpler, and more generally satisfactory for vaginal delivery than continuous caudal anæsthesia, so enthusiastically popularized a few years ago by Hingson. I am sure that the vast majority of Canadian mothers do not seek complete oblivion and amnesia for the whole period of labour, and so for first stage pain relief we do not advocate indiscriminate use of barbiturates, scopolamine or other hypnotics. Judicious administration of small doses of heroin, demerol or other analgesics, and sometimes intravenous alcohol, will usually make the pains bearable. Combined with

this there should be generous quantities of sympathetic encouragement, and an intelligently individualized psychological approach by nurses and doctors. For actual delivery, if spinal anæsthesia is not to be given, we use cyclopropane or nitrous oxide. Chloroform still has a small place in modern anæsthesia, but in my opinion should be used in obstetrics only on those infrequent occasions when there is need to relax a uterus, or to delay precipitate delivery.

Trichlorethylene or trilene is an anæsthetic agent which has been popularized in Britain for use in obstetrics. It has an excellent analgesic effect, but is not a good muscle relaxant. When used in a very dilute vapour it is apparently not very toxic. It is not suitable for administration by open drop mask or by soda-lime closed technique, and is given most satisfactorily from a specially designed inhaler, of which there are a number on the market. A simple apparatus which we have found satisfactory is that designed for the McGill Department of Anæsthesia by Asquith and Gilbert, and described in the *Canadian Medical Association Journal* of June, 1950. With such an apparatus the patient may achieve fairly satisfactory analgesia by self-administration, so that in a situation where the doctor must work without assistants trilene may be of great value. It is used also in our hospital practice to provide intermittent analgesia before the patient is ready for complete anæsthesia.

I think I have said enough about technical changes during the past few years to make it clear that safe and satisfactory modern anæsthesia requires the attention of physicians with special knowledge and skill. I do not mean to say that every doctor who gives an anæsthetic must be a certified specialist, but there is no doubt that anæsthesia is done better by those who have had some kind of special training. For this purpose training centres have been established in most of our Canadian medical schools. The first independent Department of Anæsthesia was at Laval; then in 1946 McGill, with Wesley Bourne as the first Professor. Now there are Departments also at Western, and Alberta; and subdepartments at Toronto, Manitoba, Dalhousie and Montreal. At the new Medical School of the University of British Columbia there is the nucleus for a very strong Department. At McGill, in addition to undergraduate training, we have a fully organized three-year Diploma Course, which is a combination of residency training in several co-operating hospitals with instruction in the basic science departments of the Faculty of Medicine. A somewhat similar, and very successful course, has been in operation for several years at the University of Toronto under the direction of Dr. Harry Shields. At McGill, Toronto, and elsewhere, shorter courses of varying length are also available for general practitioners or part-time specialists. In spite of all this new teaching activity the field of anæsthesiology is still wide open, with the demand for qualified doctors far greater than the supply at present or in the foreseeable future. We are losing many of our best anæsthetists to the United States where the financial inducements are most enticing. But even in Canada the outlook for young doctors in this specialty is very good indeed. I know of no other field wherein a qualified man or woman may become financially so well established so quickly. In spite of these opportunities none of our training centres is overcrowded.

A recent editorial in the *Journal of the American Medical Association* (March 24, 1951) speaks of the "Need for Anæsthesiologists" in words which could be used with almost equal validity for Canada. The editor says in part:

> "By virtue of the present outlook, anæsthesiology affords its practitioners, who are well-trained and competent, the unusual opportunity to practice a clinical specialty, with all its satisfying facets, and to utilize simultaneously much of the spectacular knowledge gained from the basic sciences. In no uncertain manner has the anæsthesiologist been transformed into a clinical physiologist and pharmacologist. During the past few years many young physicians, aware of these opportunities, have entered the specialty of anæsthesiology and have found an eminently satisfactory field of professional endeavour. . . . The community need for modern anæsthesiology is so great, however, particularly by virtue of the recent dramatic extensions of surgical treatment, that there already exists a nationwide critical shortage of bona fide anæsthesiologists. A quality of anæsthetic care commensurate with the quality of surgical care is lacking in too many localities. . . . The responsibility for obtaining more such specialists rests with the entire medical profession as well as with the relatively small number of anæsthesiologists. . . . Too many older members of the medical fraternity are not fully aware of the essential nature of the specialty and therefore are not in a valid position to encourage younger men toward this end. Yet who can deny the emergence of the anæsthesiologist as a necessary and critical participant in the joint medical effort. . . . The hospitals and the communities they serve would do well to foster and support all that is inherent in the worth-while practice of anæsthesiology."

In Canada, perhaps even more than in the United States, the field of usefulness for anæsthetists has broadened in a remarkable fashion. Preoperative evaluation and preparation of the patient; immediate postoperative care and the direction of postoperative recovery rooms;

supervision of oxygen therapy, of all sorts of intravenous therapy and of blood transfusions; bronchoscopy; diagnostic and therapeutic nerve blocks—all these are practical fields in which the anæsthetists of Canada are becoming interested. In the United States organized anæsthesiology at the present time is in the midst of an argument with hospital authorities over the question of the anæsthetist-hospital relationship. Some hospital administrators claim that anæsthesiology is a "hospital service," and believe that hospitals have a right to continue to profit financially from the collection of anæsthesiologists' fees and the employment of nurse anæsthetists. The anæsthesiologists, fully supported by the American Medical Association, state that the administration of anæsthetics is part of the practice of medicine, and that anæsthesiologists should not be considered as hospital employees.

Canadian doctors should be intelligently informed regarding this type of conflict, since it gives us a preview of what may happen when a powerful and highly organized lay group attempts to encroach upon and control the practice of medicine. With a few glaring exceptions, in Canada the anæsthetist-hospital relationship is on a satisfactory basis of mutual confidence and co-operation. If the whole profession will unite to keep it that way I believe we can look forward to maintaining world leadership in the practice, teaching, and scientific development of anæsthesia.

ASPECTS DE L'ANESTHESIE

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CE N'EST PAS sans angoisse que ceux d'entre nous, dont l'expérience professionnelle remonte au-delà de plusieurs décades, se rémémorrent leurs aventures personnelles avec le chloroforme, l'éther, ou un mélange des deux. Souventes fois l'anesthésique s'avérait un sujet d'inquiétude aussi bien pour celui qui l'administrait que pour celui qui le recevait. Pour ma part, je ne tiens pas à reprendre les combats de lutte que j'eus jadis avec des patients qui ne semblaient pas goûter que je les tinsse étouffés sous le masque. Que les temps sont changés! Nous n'avons guère plus l'occasion d'enseigner à nos étudiants la façon de donner l'éther. On peut déplorer qu'avec l'avènement des gaz et des barbiturates intraveineux on a rendu simple et facile l'induction de l'anesthésie, mais ce n'est pas le malade qui s'en plaindra. S'il sait qu'il peut s'endormir rapidement et sans malaises, assuré de ne pas se sentir souffoquer, il ne craindra pas l'anesthésie, et voilà bien qui constitue une amélioration importante de cette science.

Parmi les changements principaux survenus dans la pratique de l'anesthésie au cours des dix dernières années, je me propose de m'arrêter en particulier sur les points suivants:

(1) Usage rationnel d'anesthésiques intraveineux. (2) Introduction du curare et autres relâchants musculaires. (3) Plus grande appréciation de la valeur des gaz anesthésiants, particulièrement du protoxide d'azote. (4) La controverse: rachi-anesthésie et anesthésie générale. (5) Une meilleure anesthésie obstétricale. (6) Une meilleure formation d'anesthésistes, et un regard vers l'avenir.

Le pentothal, l'évipal, le kémital, le surital sont des dérivés de l'acide barbiturique de composition chimique légèrement différente, qui sont rapides d'action et injectés par voie intraveineuse. Administrés de façon convenable, tous s'avèrent efficaces et sûrs; par contre ils peuvent être extrêmement dangereux quand on ne prend pas les précautions voulues ou que l'on ne s'en sert pas à bon escient.

L'éther passe pour être le plus "sûr" des anesthésiques pour l'unique raison qu'à doses ordinaires il ne déprime pas la respiration. Quelle que soit la réaction des malades endormis à l'éther leur respiration ne s'arrête pas sauf parfois pour faire une pause momentanée au cours de la période d'induction. Avec les barbiturates intraveineux au contraire, surtout dans le cas d'obstruction des voies aériennes, la dépression respiratoire est le premier phénomène qui suit la perte de la connaissance.

Comme une oxygénation suffisante à travers des voies aériennes libres constitue le principe fondamental d'une anesthésie sure, il importe que tout médecin qui administre un barbiturate intraveineux ait les connaissance voulues et l'appareil nécessaire pour pratiquer le maintien artificiel de la respiration. Même s'il sert à une opération de courte durés, le pentothal, en face de ce risque possible, ne doit pas être considéré comme un "anesthésique mineur".

Les barbiturates ne sont pas de bons analgésiques, c'est pourquoi ils ne conviennent pas comme anesthésiques pour des opérations longues et douloureuses; en revanche ce sont des substances idéales pour les opérations courtes telles que la réduction de luxations, l'incision d'abcès ou l'extraction d'une ou de deux dents; souvent aussi ils servent à obtenir une induction idéale pour les opérations de longue durée. L'anesthésiste d'hôpital qui est dûment qualifié et qui a à portée de main ses ballons d'oxygène, ses tubes endotrachéaux et laryngoscopes ne redoute pas l'arrêt respiratoire parce qu'il est en mesure d'y remédier. Il lui est donc possible de se servir de barbiturates intraveineux dans des circonstances où il serait téméraire au praticien de le faire dans son bureau ou au domicile du patient.

L'introduction du curare pour le relâchement musculaire a révolutionné la pratique de l'anesthésie à l'hôpital. Cependant le fait qu'il semble endormir si facilement peut faire courir plus de risques au malade. Comme les barbiturates le curare est un déprimant respiratoire et il arrive souvent, lorsque l'on donne les deux drogues en même temps, que le patient ne respire plus spontanément pendant une demi-heure ou davantage. On voit donc combien il importe alors de savoir à fond comment assurer en tout temps le mécanisme de la respiration!

Je ne veux cependant pas donner l'impression que le curare est d'un emploi trop dangereux en clinique. Dix ans ont maintenant passé depuis que mes collégues et moi-même eurent la témérité ou la bonne fortune d'employer le curare pour obtenir le relâchement des muscles abdominaux chez nos malades endormis. C'est avec un étonnement mêlé d'humilité que nous l'avons vu se répandre à travers le monde, à tel point qu'il n'est presque plus de salle d'opération où l'on ne se sert du curare ou d'un autre agent analogue. Certes il a été cause d'accidents, même entre les mains d'experts, mais je trouve encore merveilleux qu'une aussi puissante drogue puisse d'une façon générale montrer un tel degré d'innocuité lorsqu'elle elle est administrée d'après les règles. Tant pour les chirurgiens que pour les anesthésistes, c'est une grâce et un bienfait qu'en même temps qu'une anesthésie légère on puisse obtenir un bon relâchement musculaire avec un médicament que l'on peut contrôler, qui est rapide d'action et non toxique. De nos jours les imprécations ne se font plus guère entendre dans nos salles d'opérations!

On me demande souvent mon avis au sujet de l'inoffensivité relative ou de l'efficacité des préparations courantes de curare ou de ses substituts. Nous eussions voulu nous familiariser tout à fait avec tous les aspects de la d-tubocurarine avant de faire l'essai d'autres relâchants musculaires, lesquels ont des propriétés spéciales à chacun d'eux; mais un tel espoir était vain en prévision de la valeur commerciale d'une drogue comme celle-là. Pour ce qui de la posologie des préparations telles que la syncurine, le flaxédil, la metubine, "Win 2747", la mecostrine, le decamethonium, etc., les avis sont loin d'être les mêmes, et la question de toxicité relative et de degré de dépression respiratoire fait l'object de réclames contradictoires.

Après mûre réflection je puis dire à l'heure actuelle qu'au point de vue de leur efficacité clinique ces drogues diffèrent très peu entre elles, si ce n'est peut-être dans le mécanisme de leur action physiologique. L'anesthésiste bien avisé, surtout s'il ne pratique son art qu'occasionnellement, devrait se familiariser avec une drogue à l'exclusion des autres, avec sa posologie, ses effets secondaires, comment la combiner avec d'autres anesthésiques et en neutraliser les doses trop fortes. Personnellement je donne la préférence à la d-tubocurarine, encore qu'il ne manque pas d'autres drogues qui procurent un bon relâchement musculaire.

De nos jours nous sommes plus â même de faire un choix parmi les anesthésiques, et il nous est loisible de faire une étude plus poussée des gaz, précieux à cause de leur rapidité d'action et de leur contrôle facile. Et c'est ainsi qu'on note un renouveau d'intérêt dans le protoxide d'azote pour la grande chirurgie. De tous les anesthésiques, le protoxide d'azote est le moins toxique et celui dont l'élimination se fait le plus rapidement, cependant il ne procure une anesthésie faite de quiétude et de détente qu'en y ajoutant de l'éther ou en le privant dangereusement d'oxygène. Avec le curare, on combine beaucoup d'oxigène à ce gaz même pour la chirurgie thoracique et cardiaque, aussi bien pour les enfants que pour les vieillards. A la lumière des études physiologiques et pathologiques récentes on est maintenant d'accord sur le fait que l'hypoxie peut rapidement entraîner des dommages irréparables aux cellules du cerveau, du foie, des reins et d'autres organes vitaux. L'anesthésiste se doit donc de donner avec ses drogues un volume suffisant d'oxygène, de s'assurer que cet oxygène arrive librement au contact des alvéoles pulmon-

aires, et de faire en sorte que dans le courant circulatoire il y ait un constant apport d'oxygène pour chaque cellule de l'organisme. On atteint ce but avec l'emploi judicieux de protoxide d'azote-oxygène, et aussi de l'éthylène-oxygène, et du cyclopropane-oxygène. Mon choix personnel va au cyclopropane que j'emploie dans une grande variété d'interventions chirurgicales, mais j'applaudis aussi aux efforts de ceux qui reprennent l'usage, à bon escient, du protoxide d'azote-oxygène.

L'avénement du curare a produit dans ma propre pratique un autre résultat curieux et en apparence paradoxal, à savoir une augmentation des cas de rachi-anesthésie. Mais, dira-t-on, pourquoi se servir de la technique rachidienne quand on dispose de drogues qui donnent elles aussi un bon relâchement musculaire? La seule objection logique à la rachi est le danger des complications, et puisque nous avons dans le curare un bon moyen de remédier à un relâchement que peut occasionnellement faire défaut, je soutiens qu'il est en notre pouvoir d'employer des techniques de rachi-anesthésie passablement sûres. Parmi les facteurs de sûreté, citons une technique méticuleusement soigneuse, l'emploi de petites doses de solutions diluées de drogues non toxiques, l'injection au moyen d'aiguilles fines, et un choix judicieux de cas en tenant compte des points de vue à la fois physiques et physiologiques.

On peut déduire de la mauvaise réputation faite dans les milieux mondains à la rachi-anesthésie que dans un grand nombre de cas je suis sûr qu'elle a été mal conduite. Je suis convaincu qu'elle occupe une place importante dans l'arsenal anesthésique moderne, mais qu'elle ne doit pas être laissée aux mains d'anesthésistes inexpérimentés ni réservée à des patients qui sont de "mauvais risques pour l'anesthésie générale". A l'Hôpital Homéopathique de Montréal, au cours des quatre dernières années, nous avons eu recours à la rachi-anesthésie dans 60% de nos accouchements ordinaires, ainsi que dans presque toutes nos opérations césariennes et hystérectomies. Nous tenons soigneusement compte des facteurs de sûreté déjà mentionnés et c'est soit pour cette raison soit par un heureux hasard que nous n'avons pas connu d'échecs, à la satisfaction de nos patients et de nos chirurgiens. Nous ne pouvons assurer que jamais il ne surviendra de complication neurologique, pas plus d'ailleurs qu'on ne saurait prévoir de sérieuses complications respiratoires avec l'éther ou cardiaques avec le chloroforme ou le cyclopropane. En anesthésie il n'est point de sûreté *absolue*.

Nombre de malades redoutent la rachi-anesthésie et disent préférer être endormis durant l'opération. Nous croyons aussi préférable que la plupart des opérée dorment durant une rachi-anesthésie, chose rendue facile grâce à un goutte à goutte intraveineux de pentothal à 1/500 ou à un gaz léger avec oxygène; cela vaut mieux que les bercer de paroles ou de musique, ou de les "bourrer" de morphine. On ne saurait croire combien peu d'anesthésique rachidien il faut lorsqu'on réussit à faire dormir le patient. Le seul danger à craindre dans les opérations de longue durée est de donner trop de pentothal. Pour obvier au risque d'empoisonnement par les barbiturates nous limitons arbitrairement à un gramme la dose maxima de pentothal permise en chaque cas. S'il faut pousser l'anesthésie plus avant on se servira de l'un des gaz.

Pour maintenir la tension artérielle au cours d'une anesthésie générale ou rachidienne nous comptons principalement sur les transfusions sanguines et les injections de sérum, bien qu'à l'occasion un tonique vasculaire soit indiqué. A ce propos je voudrais recommander l'emploi d'une nouvelle préparation, la methoxamine ("Vasoxyl" B. & W.), qui n'affecte pas le cœur des malades endormis au cyclopropane et qui produit à la périphérie un effet vaso-constricteur soutenu sans stimulation cérébrale. Comme tous les analeptiques elle reconnait des indications nettement définie, et ne doit jamais être donnée de façon routinière.

Le soulagement de la douleur en obstétrique semble la partie la plus négligée de l'anesthésie. De nos jours au Canada la très grande majorité des bébés naissent à l'hôpital, c'est pourquoi nous devrions parfaire nos méthodes d'anesthésie pour répondre aux besoins actuels plutôt que de perpétuer les techniques routinières qui ont cours dans les accouchements à domicile. Chaque fois que la chose est possible toute femme en travail devrait se prévaloir des services d'un anesthésiste qualifié, ou encore d'un médecin assez compétent en anesthésie moderne. Un tel service spécialisé est devenue chose courante dans notre hôpital depuis les cinq dernières années, au grand contentement à la fois des obstétriciens et des parturientes, lesquelles ne s'objectent pas à rémunérer les premiers pour des services si hautement appréciés.

Je ne tenterai pas de décrire ici toutes les techniques de l'anesthésie obstetricales. 60% des accouchement dans notre hôpital, ai-je dit, se font à la rachi-anesthésie, et le fait que nous ayons conservé cette proportion depuis longtemps prouve bien que cette méthode nous donne entière satisfaction et que chaque cas particulier est soumis à la technique qui lui convient. Il se peut que dans un autre hôpital la situation soit tout à fait différente. Le choix de la technique ou de la drogue dépend largement des méthodes obstétricales y ont habituellement cours. Un fait certain est que la rachianesthésie entraîne un usage assez fréquent du forceps, ce qui ne sort pas de l'ordinaire chez nous où nous pratiquons sur une assez haute échelle le forceps soi-disant "prophylactique".

Je crois que la rachi-anesthésie à petites doses, utilisant la procaïne à 1%, (telle que préconisée par le Dr R. J. Fraser de Hamilton), est plus simple, plus sûre et donne de meilleurs résultats dans l'accouchement ordinaire que l'anesthàsie caudale continue, rendue si populaire par Hingston il y a quelques années. Je suis d'avis que la grande majorité des mères canadiennes ne recherchent pas la perte complète de la connaissance et de la mémoire pour toute la durée du travail, en sorte que nous ne préconisons pas l'emploi sans discernement des barbiturates, de la scopolamine ou autres hypnotiques pour soulager les premières douleurs. Elles s'endureront ordinairement bien grâce à l'usage circonspect de l'héroïne, du démerol, et parfois d'alcool intraveineux. Ajoutons à cela des marques profuses de sympathique encouragement, ainsi qu'une conception psychologique intelligente de chaque cas individuel apportée par les gardes-malades et les médecins. Pour l'accouchement lui-même nous utilisons le cyclopropane ou le protoxide d'azote dans les cas où une rachi n'est pas pratiquée. Pour ce qui est du chloroforme, je crois qu'on ne doive s'en servir en obstétrique que dans ces cas peu fréquents où il importe de relâcher l'utérus ou retarder un accouchement trop rapide.

Le trichlorethylène ou trilène est un anesthésique obstétrical populaire en Grande Bretagne. Il a une action analgésiante parfaite mais ne donne pas un bon relâchement musculaire. Il ne semble pas très toxique quand il est donné sous forme de vapeur très fine. La façon la plus satisfaisante de le donner est par un inhalateur expressément fabriqué à cette fin.. Un appareil que nous trouvons très convenable est celui qui a été fabriqué par Asquith et Gilbert pour le Département d'Anesthésie de McGill, et sa description se trouve dans la livraison de juin 1950 du *Journal de l'Association Médicale Canadienne*. Grâce à cet appareil le patient peut d'administrer les drogues lui-même et s'analgésier de façon assez satisfaisante, ce qui rend le trilène très utile dans les cas où un médecin ne peut compter sur l'aide d'un assistant. Nous nous en servons aussi dans notre hôpital pour procurer une analgésie intermittente avant que le patient ne soit prêt pour l'anesthésie complète.

Je crois en avoir assez dit sur l'évolution des techniques au cours des dernières années pour en conclure qu'il ne saurait de nos jours y avoir d'anesthésie sûre et satisfaisante sans l'apport de médecins compétents et expérimentés. Cela ne veut pas dire que tout docteur qui donne un anesthésique soit être un spécialiste qualifié, mais l'anesthésie n'en sera certainement mieux faite que s'il a déjà reçu quelques entraînement. C'est dans ce but que la plupart des écoles de médecine canadiennes ont institué des centres d'entraînement. Laval fonda le premier départe-d'Anesthésie, puis ce fut McGill en 1946 avec Wesley Bourne comme premier professeur. Il en est maintenant en Alberta et au Western, puis aux Universités de Toronto, Manitoba, Dalhousie et Montréal. A la nouvelle Ecole de Médecine de l'Université de Colombie Britannique on est à instituer un important service. A McGill, outre l'entraînement médical, nous avons le cours de trois ans avec obtention de diplôme, et qui consiste à la fois en un entraînement comme médecin résident dans un hôpital qualifié et en des cours dans le département d'anesthésie à la Faculté de Médecine. A l'Université de Toronto un cours semblable, sous la direction du Dr Harry Shields, connait un grand succès depuis plusieurs années. D'autres cours de plus courte durée se donnent à McGill, Toronto et ailleurs pour les praticiens et spécialistes à temps partiel.

En dépit de toute cette effervescence d'enseignement l'étude de l'anesthésie s'ouvre à tous, tellement est grand aujourd'hui et sera sûrement aussi demain le besoin de médecins qualifiés en cette science. Plusieurs de nos meilleurs anesthésistes nous quittent pour les Etats-Unis où ils sont attirés par de plus substantiels émoluments; au Canada cependant les jeunes médecins peuvent beaucoup espérer de cette spécialisation. Il n'est pas d'autre branche de la médecine ou un homme ou une femme qualifiés peuvent se faire d'intéressants revenus aussi rapidement, et

cependant la place ne manque jamais dans nos centres d'entraînement.

Dans un récent éditorial du *Journal de l'American Medical Association* (24 mars 1951), on traite du "Besoin d'Anesthésistes" en des termes qui valent également pour le Canada. On y lit, en partie:

"Dans l'état actuel des choses, l'anesthésiologie fournit à ses adeptes, qui sont compétents et bien entraînés, une occasion peu banale de pratiquer une spécialité médicale dont les facettes sont des plus reluisantes, et d'utiliser en même temps maintes connaissances précieuses puisées à même la science médicale de base. Sûrement ainsi l'anesthésiste est transformé en un physiologue clinique et en un pharmacologue. Bien au courant de ces faits, nombre de jeunes médecins ont depuis quelques années embrassé la carrière d'anesthésiste et y ont trouvé un champ professionnel des plus fertiles. . . . A cause des progrès étonnants de la chirurgie moderne, le besoin de spécialistes connaissant à fond l'anesthésie se fait de plus en plus pressant à travers toute la nation. Dans trop de localités il n'existe pas de soins anesthésiques se rapprochant par la qualité des soins chirurgicaux même. . . . C'est à la profession médicale entière et au nombre relativement peu élevé d'anesthésistes que revient la responsabilité d'obtenir plus de spécialistes en cette branche. . . . Trop de médecins parmi les plus âgés ne réalisent pas assez le rôle essentiel de la spécialité pour encourager leurs confrères plus jeunes dans cette voie. Et cependant dans l'effort médical commun l'anesthésiste prend aujourd'hui une part de plus en plus nécessaire et décisive. . . ."

Au Canada plus encore peut-être qu'aux Etats-Unis le champ d'utilité pour les anesthésistes s'est élargi de façon remarquable. Préparation du malade et étude se son état préopératoire; soins postopératoires immédiats et direction des chambres de réveil postopératoire; haute surveillance de l'oxygénothérapie, de toutes les variétés de traitements intraveineux et des transfusions sanguines; bronchoscopie; blocage de nerfs pour fins diagnostiques ou thérapeutiques—voilà autant de pratiques auxquelles s'intéressent de plus en plus les anesthésistes canadiens. Aux Etats-Unis on est en train présentement de débattre la question des rapports entre l'anesthésiste et l'hôpital. Certains administrateurs d'hôpital estiment que l'anesthésie est un "service de l'hôpital" et que les institutions hospitalières ont le droit de participer aux honoraires des anesthésistes et tirer profit de l'emploi des infirmières anesthesistes. En revanche, et avec le plein appui de l'American Medical Association, les anesthésistes soutiennent que l'administration des anesthésiques des anesthésiques fait partie de la pratique de la médecine, et qu'ils ne devraient point être considérés comme des employés d'hôpitaux.

Un tel conflit devrait être étudié sérieusement par les médecins canadiens, car il nous fait entrevoir ce qui peut arriver lorsqu'un groupement laïque fort et bien organisé tent d'empiéter sur la pratique de la médecine et la subjuguer. Sauf quelques exceptions notoires, ici au Canada administrateurs d'hôpital et anesthésistes se font mutuellement confiance et coopèrent bien entre eux. Et pour peu que la profession médicale tout entière garde ainsi un front uni nous pouvons espérer rester au tout premier plan dans le monde pour ce qui a trait à la pratique, à l'enseignement et au développement scientifique de l'anesthésie.

ACCIDENTS IN CHILDREN*

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EVERY YEAR approximately 1,500 Canadian children die as the result of accidents, a mortality greater than that due to the ten acute infectious diseases of childhood combined. In the past few decades the medical profession has put great emphasis on the reduction of mortality due to these infectious diseases, but during the same period has put relatively little emphasis on accidents. Most accidents are preventable. The physician, therefore, in his unique position as a family counsellor from the birth of the child throughout that child's development to adulthood, has not only a great opportunity to prevent accidents by education of the parents and the child, but also has a grave responsibility to do so. In this lies one of the greatest hopes of preventing this needless waste of life. For this reason it is thought worthwhile to analyze accidental deaths in Canadian children and thereby show where the challenge lies. The figures tabulated were obtained from the Vital Statistics of Canada.[1]

Tables I and II show the causes of death in children throughout Canada during the two five-year periods of 1922-26 and 1942-46 inclusive. Table I shows that in the period 1922-26, accidents stand in seventh place as a cause of death in children from birth up to the fifteenth birth-

*From the Hospital for Sick Children and the Department of Pædiatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P.[C.].

TABLE I.

CAUSES OF DEATH IN CHILDREN IN CANADA 1922-26 INCLUSIVE*

	Under 1 year	*1 year*	*2 years*	*3 years*	*4 years*	*5-9 years inclusive*	*10-14 years inclusive*	*Birth-14 years inclusive*
Acute infectious disease of childhood†	3,555	1,993	1,126	883	806	2,473	898	11,734
Tuberculosis	726	568	344	251	208	851	1,108	4,056
Other infectious diseases	3,793	1,079	462	302	198	712	578	7,124
Cancer and other tumours	22	24	33	15	24	62	54	234
Acute rheumatic fever	6	6	9	30	22	166	210	449
Blood diseases	254	72	45	23	21	87	67	569
Diseases of the nervous system	3,459	751	287	199	157	566	430	5,849
Diseases of the heart and circulatory system	185	75	60	52	68	417	521	1,378
Diseases of the respiratory system	9,854	2,876	1,019	535	360	911	430	15,985
Diseases of the digestive system	12,610	1,940	744	522	373	1,233	903	18,325
Miscellaneous, cause known‡	38,922	592	240	164	136	503	540	41,097
Accidental deaths	618	616	578	468	365	1,279	1,080	5,004
Ill defined and unknown	2,310	394	110	85	51	137	104	3,191
Total deaths	76,314	10,986	5,057	3,529	2,789	9,397	6,923	114,995

*Registration area did not include the Province of Quebec for 1922-25 inclusive, but did include Quebec for 1926. A breakdown of the statistics for each of these years reveals that the death rates are not appreciably altered by the omission of the Province of Quebec during the first four years.

†Cerebrospinal meningitis, scarlet fever, whooping cough, diphtheria, measles, poliomyelitis, German measles, Chicken-pox, mumps and smallpox.

‡Rheumatism (other than rheumatic fever); diseases of nutrition; diseases of the endocrine glands; chronic poisonings, diseases of the urinary and genital systems; diseases of pregnancy, childbirth and the puerperal state; skin diseases; diseases of the bones and organs of movement; congenital malformations; diseases peculiar to the first year of life; suicides and homicides.

day. During each successive year from birth to the fifth birthday, they increase from ninth to third place as a cause of death; and in the five to nine and ten to fourteen year age groups they are second as a cause of death for each year. In children over the age of one year, 11% of deaths are due to accidents. Table II shows that a remarkable change has occurred by the time the 1942-46 period is reached. Accidents now stand in fourth instead of seventh place as a cause of death in children. During the first year they stand in eighth place, during the second year in third place, and during each year after infancy in first place. Now in children over

TABLE II.

CAUSES OF DEATH IN CHILDREN IN CANADA—1942-46 INCLUSIVE

	Under 1 year	*1 year*	*2 years*	*3 years*	*4 years*	*5-9 years inclusive*	*10-14 years inclusive*	*Birth—14 years inclusive*
Acute infectious diseases of childhood†	2,258	747	406	323	278	821	277	5,110
Tuberculosis	582	490	346	281	194	872	1,010	3,775
Other infectious diseases	3,291	606	248	179	116	351	243	5,034
Cancer and other tumours	41	84	86	78	72	243	181	785
Acute rheumatic fever	8	5	7	17	28	203	222	490
Blood diseases	127	115	81	83	55	177	141	779
Diseases of the nervous system	2,524	515	229	177	140	370	296	4,251
Diseases of the heart and circulatory system	12	46	34	32	35	193	262	614
Diseases of the respiratory system	10,993	1,730	632	359	220	505	313	14,752
Diseases of the digestive system	8,974	1,069	424	376	303	790	581	12,517
Miscellaneous, cause known‡	43,558	616	267	195	129	473	475	45,713
Accidental deaths	1,375	798	783	645	539	1,738	1,437	7,315
Ill defined and unknown	1,921	204	79	35	28	115	48	2,430
Total deaths	75,664	7,025	3,622	2,780	2,137	6,851	5,486	103,565

the age of one year 21% of deaths are due to accidents.

Although these tables do not take into account the great increase in population between the two periods, it is apparent from a study of the tables that the increasing importance of accidents is due in large part to a decrease in deaths due to the acute infectious diseases of childhood, tuberculosis, the other infectious diseases and diseases of the respiratory, circulatory, nervous and digestive systems, rather than to a great increase in accidental deaths.

TABLE III.

POPULATION OF CANADA (ESTIMATED)

Year	*Population*
1922	6,507,000*
1923	6,577,000*
1924	6,659,000*
1925	6,737,000*
1926	9,439,000
1942	11,637,000
1943	11,795,000
1944	11,958,000
1945	12,102,000
1946	12,283,000

*Does not include Province of Quebec.

Table III shows the estimated population of Canada for each of the years under study. On the basis of these estimates the total accidental deaths and the total deaths, both accidental and non-accidental, are further analyzed in Table IV, according to rate per 10,000,000 population. These figures show a tremendous decrease in total deaths for all age groups with an over-all reduction of 45%. Accidental deaths show an increase during the first year but a decrease in all other age groups. However, the over-all reduction in the accidental death rate is only 12%.

In Tables V and VI the accidental deaths are further analyzed according to the type of accident. In the 1922-26 period drownings stand first as a cause of death, accidents of transportation second and burns third. In the 1942-46 period accidents of transportation stand first with drownings second. Table VII compares these same accidental deaths according to rate per 10,000,000 population. This table reveals a considerable increase in deaths due to accidents of transportation, but large decreases in deaths due to poisonings, burns, drownings, firearms and falls and crushings.

TABLE IV.

TOTAL AND ACCIDENTAL DEATHS IN CHILDREN IN CANADA, BY YEAR (RATE PER 10,000,000 POPULATION)

	Year	*Under 1 year*	*1 year*	*2 years*	*3 years*	*4 years*	*5-9 years inclusive*	*10-14 years inclusive*	*Birth-14 years inclusive*
Total accidental deaths	1922	148	180	165	122	112	390	320	1,437
	1923	167	184	178	133	104	371	283	1,420
	1924	190	169	134	142	106	284	289	1,314
	1925	190	163	158	136	87	380	313	1,427
	1926	168	166	169	123	99	360	298	1,383
	Average	173	172	161	131	102	357	301	1,396
Total deaths accidental and non-accidental	1922	22,000	2,900	1,460	940	820	3,000	2,000	33,120
	1923	21,000	3,000	1,340	940	690	2,750	1,860	31,580
	1924	18,700	2,570	1,220	980	840	2,450	1,910	28,670
	1925	18,100	2,380	1,140	850	675	2,200	1,810	27,155
	1926	25,000	4,000	1,730	1,140	875	2,650	2,040	37,435
	Average	20,960	2,970	1,380	970	780	2,610	1,925	31,592
Total accidental deaths	1942	205	129	140	121	87	258	221	1,161
	1943	250	131	137	118	102	314	271	1,323
	1944	215	134	134	94	96	315	251	1,239
	1945	225	148	118	98	78	278	234	1,179
	1946	250	126	126	109	88	287	222	1,208
	Average	229	134	131	108	90	290	240	1,222
Total deaths accidental and non-accidental	1942	12,600	1,300	710	520	415	1,180	1,000	17,725
	1943	12,900	1,210	625	440	365	1,250	1,040	17,830
	1944	13,000	1,270	605	475	375	1,230	925	17,880
	1945	12,300	1,020	515	435	305	1,020	830	16,425
	1946	12,500	1,080	525	420	335	1,060	800	16,720
	Average	12,660	1,176	596	458	359	1,148	919	17,316

TABLE V.

ACCIDENTAL DEATHS IN CHILDREN IN CANADA 1922-26 INCLUSIVE

Cause of death	*Under 1 year*	*1 year*	*2 years*	*3 years*	*4 years*	*5-9 years inclusive*	*10-14 years inclusive*	*Birth-14 years inclusive*
Railway, motor vehicle and other road, water and air transport accidents	29	45	53	80	92	381	241	921
Acute accidental poisonings by solids and liquids	43	92	62	47	19	37	21	321
Conflagration	34	40	38	37	33	79	50	311
Burns other than conflagration	83	206	225	131	93	125	39	902
Drownings	19	116	99	89	67	361	401	1,152
Firearms	1	2	11	6	8	46	106	180
Falls and crushings	37	36	37	28	18	96	76	328
Electric currents	0	0	0	1	0	4	9	14
Obstruction, suffocation or puncture by ingested objects	320	27	15	3	8	8	5	386
Miscellaneous	52	52	38	46	27	142	132	489
Total accidental deaths	618	616	578	468	365	1,279	1,080	5,004
Total deaths from all causes, accidental and non-accidental	76,314	10,986	5,057	3,529	2,789	9,397	6,923	114,995

A study of fatal accidents involves only one phase of the accident problem, since for each fatal accident there are a great many non-fatal yet disabling accidents which result in serious illness and often permanent crippling. Unfortunately, accurate statistics on non-fatal accidents are unobtainable on a country-wide basis. In the United States it is estimated that for every death from a home accident, some 150 additional disabling accidents occur.[2]

TABLE VI.

ACCIDENTAL DEATHS IN CHILDREN IN CANADA 1942-46 INCLUSIVE

Cause of death	*Under year*	*1 year*	*2 years*	*3 years*	*4 years*	*5-9 years inclusive*	*10-14 years inclusive*	*Birth-14 years inclusive*
Railway, motor vehicle and other road, water and air transport accidents	33	107	196	234	237	853	482	2,142
Acute accidental poisonings by solids and liquids	21	101	62	35	11	10	6	246
Conflagration	84	89	101	81	73	121	59	608
Burns other than conflagration	65	126	127	79	44	76	34	551
Drownings	18	149	164	122	102	415	453	1,423
Firearms	0	4	0	8	5	38	103	158
Falls and crushings	52	67	41	33	20	90	100	403
Electric currents	1	2	2	0	1	7	12	25
Obstruction, suffocation or puncture by ingested objects	416	73	32	8	10	6	7	552
Miscellaneous	685	80	58	45	36	122	181	1,207
Total accidental deaths	1,375	798	783	645	539	1,738	1,437	7,315
Total deaths from all causes, accidental and non-accidental	75,664	7,025	3,622	2,780	2,137	6,851	5,486	103,565

TABLE VII.

ACCIDENTAL DEATHS IN CHILDREN IN CANADA BY YEAR
RATE/10,000,000 POPULATION/YEAR

Cause of death	*1922–6 inclusive*	*1942–6 inclusive*
Railway, motor vehicle and other road, water and air transport accidents	253	358
Acute accidental poisonings by solids and liquids	88	41
Conflagration	87	102
Burns other than conflagration	249	92
Drownings	324	238
Firearms	51	27
Falls and crushings	91	67
Electric Currents	4	4
Obstruction, suffocation or puncture by ingested objects	110	92
Miscellaneous	136	202
Total accidental deaths	1,396	1,222

The most reliable statistics obtainable on non-fatal accidents are probably those obtained from hospital records. Table VIII lists the number of admissions to the Hospital for Sick Children, Toronto, because of accidents, during the five-year period 1943-47 inclusive. These figures show that among those children injured seriously enough to be admitted to hospital, the mortality rate is less than 1%.

TABLE VIII.

ADMISSIONS TO THE HOSPITAL FOR SICK CHILDREN, TORONTO
1943-47 INCLUSIVE, BECAUSE OF ACCIDENTS

	Number of admissions	*Number of deaths*
Burns and scalds	644	12
Wringer injuries	132	0
Head injuries	1,345	30
Lacerations	765	2
Fractures	2,381	2
Poisonings	141	0
Total	5,408*	46

*Because of more than 1 diagnosis in some patients, this total represents approximately 5,000 patients.

SUMMARY

A statistical review is given of the causes of death among Canadian children during the years 1922-26 and 1942-46 inclusive. These figures show that during this twenty-year period, due to a decrease in fatalities from disease, accidents have risen to first place as a cause of death in children past infancy and during the age group two to fourteen years inclusive account for 21% of deaths.

These accidental deaths are further analyzed according to rates per unit population and according to type of accident.

It is pointed out that one of the chief hopes for a reduction in fatalities due to accidents lies with the physician, who, when aware of the importance of accidents as a leading cause of death, can, by the education of parents and children, make a great contribution towards the reduction of this mortality.

REFERENCES

1. Vital Statistics of Canada 1922-26 and 1942-46 inclusive.
2. Accidents, Childhood's Greatest Hazard. Transactions 1950 National Safety Congress, U.S.A.

PROBLEM CASES.—As a young pharmacist I often observed that many physicians tried to avoid taking patients who were hard to handle, or they tried to get rid of such individuals at the earliest opportunity. When I stepped out of the station in the city where I was to study medicine, I saw across the street a large sign for Pickwick Clothing. Their slogan was "We fit the hard to fit." It occurred to me that here was a firm that had made an immense success by not only catering to but actually inviting, the problem individuals in their field. It not only suggested to me the advantage of being a "Pickwick Doctor" but has largely influenced some of my attitudes since that time. Whenever I have failed to make good with a problem case, I have felt a distinct sense of personal failure.—Bethea, O. W., Medical Ethics, *The Mississippi Doctor*, **28**: 372, 1951.

MEDICAL RESEARCH.—We ought first to note the rapid spread—thinking of Harvey, we ought to call it a revival, perhaps—of the belief that a direct study of the disease in the human patient can partake of the nature of a genuinely scientific research. It may be purely observational, it may be experimental in its method; but, in either case, it is ready now to accept the controls and submit to the discipline of the scientific method, and no longer seeks escape from these on a plea that medicine is, and, by implication, can be content to remain, an empirical art and not a science.—Sir Henry Dale, Scientific Method in Medical Research, *Brit. M. J.*, p. 1187, November 25, 1950.

STUDIES ON POLIOMYELITIS IN ONTARIO*

V. Further Observations on the Recovery of Coxsackie Viruses from Cases of Clinical Poliomyelitis

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IT IS NOW WELL RECOGNIZED that infections with Coxsackie virus may closely simulate poliomyelitis, and it is probable that many patients diagnosed clinically as suffering from abortive or non-paralytic ("meningeal") poliomyelitis are in reality infected with this newly described agent.[1 to 10]

The rôle of Coxsackie virus in causing frank paralysis is not yet elucidated, although the original strains were recovered from the stools of 2 children with muscular weakness.[11, 12] Of particular interest in this connection are reports that both Coxsackie and poliomyelitis viruses have been recovered from the same stool specimen of certain patients.[9, 13 to 17] Such double isolations have been made from healthy carriers; persons with "minor illnesses"; cases of benign aseptic, serous, or lymphocytic meningitis; and patients with spinal or bulbar paralysis.

In Toronto, we have for some years been interested in the problem of the differentiation of poliomyelitis from poliomyelitis-like illnesses, and have carried out several studies in this connection.[15 to 20] This work has been continued, and the present report describes the results of a rather detailed examination by clinical and laboratory methods of about 20 children admitted to the Hospital for Sick Children, Toronto during the summer and fall of 1950. This study was undertaken to obtain some information regarding the frequency of Coxsackie infections among cases of apparently typical non-paralytic as well as paralytic poliomyelitis. Another aspect of the investigation was the correlation of the findings on clinical examination with the results of laboratory tests, for it would obviously be of great help to the clinician if cases of Coxsackie infection could be differentiated from poliomyelitis by means other than those of the laboratory. It is a serious disadvantage that laboratory tests require several weeks or often months for completion.

From the 22 patients studied, 8 strains of Coxsackie virus were recovered. Additional evidence for the prevalence of Coxsackie infections in Toronto in 1950 was afforded by the results of examinations of Toronto City sewage, as Coxsackie virus was recovered in June and in September from this source.[21]

METHODS

Clinical Study

From May to November, 1950, all patients admitted to the Hospital for Sick Children with a clinical diagnosis of poliomyelitis were examined daily during their stay in hospital by two of us (C.A. and J.B.J.McK.). Examinations of the cerebrospinal fluid and peripheral white blood counts were performed in the routine laboratories of the Hospital. Specimens of acute and convalescent phase serum, stools, and throat washings were obtained from as many as possible of these children, and stored in the frozen state pending testing in the virus laboratories.

VIRUS LABORATORY INVESTIGATIONS

Virus isolations.—Tests for the presence of Coxsackie and poliomyelitis viruses were performed by inoculating stool extracts prepared by ultracentrifugation cerebrally in suckling mice and rhesus monkeys. Since our technical methods have been described recently, only brief details need be given here.[17] The final diagnosis of Coxsackie or poliomyelitis infection was made on the results of histological examinations.[2, 22]

If a specimen of stool failed to produce histologically typical poliomyelitis in the first rhesus monkey, a second animal was injected with freshly prepared extract treated by ultracentrifugation; in some cases, extracts prepared from the stools of individual patients were pooled for this purpose.

In order that tests might be carried out for the presence of homologous Coxsackie antibody in acute and convalescent serum, it was necessary to prepare pools of the eight strains that were isolated. Some of these strains had to be passed cerebrally through suckling mice for a few transfers, in order to insure that the preparations were fully virulent. To date we have worked in detail only with 6 strains producing characteristic myositis in 3 day old mice. Two additional strains do not cause myositis but produce lesions in the fat and brain. These strains are being further studied.

Pools of virus were prepared by inoculating suckling mice (3 days old) cerebrally. The mice were sacrificed at the first signs of illness, usually between 2 and 5 days after inoculation. With sterile precautions, the skin was removed, the head cut off, and the carcass eviscerated. The carcasses of 20 or more animals were disintegrated mechanically in a Waring blender, suspended in physio-

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logical saline to a final 20% suspension, and then centrifuged at 1,500 r.p.m. for 3 minutes. The supernatant fluid was distributed to screw-capped vials as "virus pool" and stored in the frozen state.

Each pool so prepared was titrated in suckling mice, at least twice, before use in serum diagnostic tests. In the first titration, ten-fold dilutions of pool were inoculated intracerebrally (0.03 ml.) into a litter of 8 or 9 three day old suckling mice. The mice were observed closely and the deaths in each group recorded. Then, with knowledge of the approximate virus titre, a second titration was carried out in which the virus was prepared in "half-log" dilutions around the approximate endpoint. Fifty per cent lethal doses (LD_{50}) were calculated either by plotting probits of mortalities of groups of mice inoculated with the various dilutions of virus, or by employing Karber's method. All pools were also demonstrated to be non-pathogenic for adult mice.

SEROLOGICAL TESTS

When pools of the various Coxsackie viruses isolated from the patients had been prepared and titrated as described, it was possible to proceed with virus neutralization tests. With some modifications, these tests were conducted by a method similar to that recommended by other workers.[2, 23, 24] The object of these tests was to examine the acute and convalescent phase serum of each patient, proved to be excreting Coxsackie virus, against the homologous virus isolated from the stool. In this way, it was possible to investigate whether a rise in serum antibody level developed in convalescence from the illness in question.

Detailed studies are now in progress in which the Toronto 1950 strains mentioned in this paper are being tested with immune sera prepared to strains of Coxsackie virus recovered by Dalldorf, Melnick and others. The results of these tests will be reported later.

Virus neutralization tests were carried out by preparing serial ten-fold dilutions in saline of the acute and convalescent phase sera, and adding to neat serum and each dilution thereof an equal volume of a fixed dose of homologous virus pool. The final concentration of virus in the virus-serum mixtures was usually approximately 100 LD_{50}. At the same time, control mixtures of normal serum and virus were prepared. Virus-serum mixtures were allowed to stand at room temperature for at least 30 minutes before inoculation into one litter of three day old suckling mice (0.03 ml. intracerebrally). The suckling mice used for these tests were apportioned to mothers at random, in order to minimize possible variations in susceptibility of individual litters. A titration of the virus pool used was also carried out.

Mouse deaths were duly recorded, and the 50% neutralizing (protective) endpoint of the serum calculated by the methods already mentioned. The 50% neutralizing endpoint is defined as that dilution of serum, before admixture with an equal volume of virus, which protects 50% of inoculated mice from death.

Through the kind collaboration of Dr. Sigel, Children's Hospital, Philadelphia, it was possible to have many of the patients' sera examined for antibodies to mumps and lymphocytic choriomeningitis viruses.

RESULTS

Clinical Study

A detailed study was made of all 45 patients admitted to the hospital with a clinical diagnosis of poliomyelitis. In addition to a daily clinical investigation, peripheral white blood cell counts and cerebrospinal fluid examinations were made.

At the close of the poliomyelitis "season", the cases were all reviewed in the light of the clinical course of the illness, and 22 were selected for study by virus laboratory methods, mainly on the basis of there being available suitable specimens collected within about 10 days of the onset of illness. These 22 cases were made up of 3 with bulbar paralysis, 7 with spinal paralysis, 1 with ascending paralysis, and 11 with the non-paralytic variety of the illness.

It eventually transpired that 8 of these patients (2 spinal paralytic, 1 bulbar, and 5 non-paralytic) were excreting Coxsackie virus, as will be described in the next section; the 3 paralytic cases also excreted poliomyelitis virus, but the non-paralytic patients did not. The case histories of all 22 patients were then carefully reviewed, with the object of seeing whether any differentiation could be made on clinical grounds between those excreting Coxsackie virus and those who did not excrete this agent. No difference could be found in the clinical features, course of illness, or prognosis in the two groups, and the findings were typical of poliomyelitis. The number of cases involved is of course small, and it is possible that with large numbers some differentiation might be made between illnesses associated with the Coxsackie virus and those associated with poliomyelitis. During the 1951 poliomyelitis "season" in Toronto we intend to renew our investigations on a more detailed scale, with additional examinations by electrocardiographic, hæmatological, and biochemical methods.

For completeness, the clinical histories, in summarized form, of the 8 patients excreting Coxsackie virus are now given.

1. J.B., age 3 years, female.
   Admitted, May, 1950.
   History: Fever, vomiting, irritability, pain R. leg, not walking, for 8 days prior to admission.
   Physical examination: Neck rigidity, muscle tenderness, weakness of R. hip flexors, adductors, rotators, hamstrings, calf and anterior tibial muscles. On the L. side, weakness of hip flexors.
   Laboratory data: *Blood*, W.B.C., 9,800 (neutrophils, 34%, lymphocytes, 64%, monocytes, 2%).
   C.S.F., 30 cells, all lymphocytes; protein 73 mgm. %.
   Clinical course: Gradual improvement, but weakness still present in R. and L. hip and R. leg muscles; now walking.
   Clinical diagnosis: Spinal poliomyelitis.

2. D.S., age 2½ years, female.
   Admitted, July, 1950.
   History: Fever and upper respiratory infection 9 days prior to admission. Not moving L. arm, 5 days prior to admission.
   Physical examination: Post-nasal discharge, reflexes intact, neck rigidity, L. deltoid paralysis.
   Laboratory data: *Blood*, W.B.C., 10,400 (neutrophils, 55%, lymphocytes, 41%, monocytes, 1%).
   C.S.F., 10 cells, all lymphocytes; protein 22 mgm. %.
   Clinical course: Gradual improvement over period of 2 months. Complete recovery on discharge.
   Clinical diagnosis: Spinal poliomyelitis.

3. C.B., age 7 years, female.

Admitted, August, 1950.
History: Sore throat, temperature of 99° F., drowsiness, for 3 days prior to admission. Gradually became semi-comatose.
Physical examination: Reflexes intact, neck and back rigidity, semi-comatose for 3 to 4 days, during which time R. facial muscle weakness occurred.
Laboratory data: *Blood*, W.B.C., 5,400.
C.S.F., 130 cells, lymphocytes, 80%, protein, 29 mgm. %.
Clinical course: In 7 days, patient normal apart from R. facial weakness. Still R. facial weakness 2 weeks after discharge, no other sequelæ.
Clinical diagnosis: Bulbar poliomyelitis.

4. A.P., age 3½ years, male.

Admitted, June, 1950.
History: Fever, vomiting, constipation, drowsiness, general weakness, for 2 days prior to admission.
Physical examination: Reflexes active; neck and back muscle rigidity.
Laboratory data: *Blood*, W.B.C., 7,800.
C.S.F., 80 cells, 80% lymphocytes.
Clinical course: All symptoms and fever subsided during 7 days in hospital. Two weeks later, no sequelæ.
Clinical diagnosis: Non-paralytic poliomyelitis.

5. L.B., age 4 years, female.

Admitted, August, 1950.
History: Temperature of 101° F., vomiting, stiff neck, listlessness, for 2 days prior to admission.
Physical examination: Reflexes intact, minimal neck rigidity.
Laboratory data: *Blood*, W.B.C., 4,600 (neutrophils, 65%, lymphocytes, 29%, monocytes, 4%).
C.S.F., 31 cells, lymphocytes, 95%.
Clinical course: Discharged in 7 days, completely recovered. Two weeks later, no sequelæ.
Clinical diagnosis: Non-paralytic poliomyelitis.

6. M.T., age 8 years, female.

Admitted, August, 1950.
History: Headache, fever, sore neck, for 1 day prior to admission.
Physical examination: Reflexes intact, minimal neck rigidity.
Laboratory data: *Blood*, W.B.C., 15,100 (neutrophils, 75%; lymphocytes, 19%, monocytes, 6%).
C.S.F., 19 cells, lymphocytes, 88%.
Clinical course: Discharged in 7 days, completely recovered. Two weeks later, no sequelæ.
Clinical diagnosis: Non-paralytic poliomyelitis.

7. R.C., age 9 years, male.

Admitted, July, 1950.
History: Headache, fever, vomiting, for 7 days prior to admission. "Dromedary" type of illness.
Physical examination: Reflexes intact, no rigidity.
Laboratory data: *Blood*, W.B.C., 8,900 (neutrophils, 48%, lymphocytes, 44%, monocytes, 4%).
C.S.F., 120 cells, all lymphocytes; protein 42 mgm. %.
Clinical course: Symptoms subsided in 7 days. Two weeks later, no sequelæ.
Clinical diagnosis: Non-paralytic poliomyelitis.

8. R.R., age 6 years, male.

Admitted, August, 1950.
History: Temperature of 103° F., pain in neck and abdomen, for 3 days prior to admission.
Physical examination: Reflexes intact, minimal neck rigidity.
Laboratory data: *Blood*, W.B.C., 7,500 (neutrophils, 60%, lymphocytes, 39%, monocytes, 1%).
C.S.F., 15 cells, lymphocytes, 90%, protein 24 mgm. %.
Clinical course: Discharged in 7 days, completely recovered. Two weeks later, no sequelæ.
Clinical diagnosis: Non-paralytic poliomyelitis.

Special mention should be made of the case of L.D., a 9 month infant who suffered from an ascending paralysis involving the legs, arms, and head. This child eventually recovered completely. A diagnosis of poliomyelitis was scarcely considered at the time, but later it was found that she was excreting poliomyelitis virus in the stool; no Coxsackie virus was isolated. The details of this patient are as follows:

L.D., age 9 months, female.
Admitted, October, 1950.
History: Temperature of 103° F., vomiting, irritability, for 7 days prior to admission. Unable to sit up 5 days before admission; then unable to move legs, then arms, and finally unable to hold up head.
Physical examination: No reflexes elicited, generalized muscle hypotonia, upper and lower extremities moved weakly, L. arm and leg weaker than R.
Laboratory data: *Blood*, W.B.C., 11,000.
C.S.F., 6 cells, protein, 49 mgm. %.
Clinical course: Irritability subsided; gradual improvement in muscle weakness but still marked at time of discharge 3 weeks later.
Clinical diagnosis: Ascending paralysis, etiology in doubt.

LABORATORY INVESTIGATIONS

Virus isolations.—The results of inoculating into suckling mice and rhesus monkeys extracts of stools of 10 children suffering from clinically typical paralytic poliomyelitis and 1 child with an ascending paralysis are shown in Table I. It will be seen that 3 strains of Coxsackie virus were isolated, one of these being from a case with bulbar involvement. These strains all produced well-marked myositis in 3 day old mice. Poliomyelitis virus was recovered from the stools of all of the 11 patients. This high recovery rate is attributable to the use of ultracentrifuged stool extracts, and the selection of specimens obtained within a short time of onset of illness. Both Coxsackie and poliomyelitis viruses were therefore recovered from 3 patients (J.B., D.S. and C.B.).

The results of inoculating stool extracts from 11 children suffering from clinically typical non-paralytic poliomyelitis are shown in Table II.

TABLE I.

RESULTS OF TESTS FOR COXSACKIE AND POLIOMYELITIS VIRUSES, PARALYTIC POLIOMYELITIS, HOSPITAL FOR SICK CHILDREN, SUMMER 1950

Patient, age (in years)	*Type of illness**	*Interval between onset of illness and stool collection (in days)*	*Result of inoculating stools in*	
			Suckling mice for Coxsackie virus	*Monkey for poliomyelitis virus*
J.B. 3	P.	8	+	880 +
D.S. 2½	P.	9	+	859 +
C.B. 7	B.	4	+	923 +
J.B. 3	P.	9	—	912 +
C.A.V. 2½	P.	4	—	904 +
J.G. 10	B.	5	—	908 +
D.C. 7	B.	1	—	910 +
J.P. 2	P.	10	—	905 +
J.D. 5	P.	12	—	858 +
R.W. 8	P.	4	—	901 +
L.D. 9/12	A.P.	8	—	892 +
Total Positive			3/11	11/11

*P = Paralytic.
B = Bulbar.
AP = Ascending paralysis.

TABLE II.

RESULTS OF TESTS FOR COXSACKIE AND POLIOMYELITIS VIRUSES, NON-PARALYTIC POLIOMYELITIS, HOSPITAL FOR SICK CHILDREN, SUMMER 1950

Patient, age (in years)	*Interval between onset of illness and stool collection (in days)*	*Result of inoculating stools in*		
		Suckling mice for Coxsackie virus	*Monkeys for poliomyelitis virus*	
			Monkey 1	*Monkey 2*
A.P. 3½	14	+	860 –	903 –
L.B. 4	3	+	873 –	913 –
M.T. 8	3	+	909 –	924 –*
R.C. 9	1	+	902 –	924 –*
R.R. 6	6	+	921 –	
J.C. 7	2	—	872 –	919 –
C.S. 5	1	—	918 –	924 –*
J.L. 5½	9	—	874 –	924 –*
K.Z. 3	4	—	881 –	924 –*
H.M. 7	5	—	896 –	916 –
D.C. 12	3	—	891 –	924 –*
Total positive		5/11	0/11	

*These specimens were pooled for inoculation of monkey No. 2.

Five strains of Coxsackie virus were recovered; 3 produced typical myositis, and 2 produced involvement of fat and brain (R.C., R.R.). No poliomyelitis virus was isolated from any patient, even though 2 monkeys were used in all except one case, and the specimens were collected shortly after the onset of illness. This finding is in marked contrast to the results with paralyzed patients (11/11 positive).

SEROLOGICAL TESTS

Tests for antibody to the homologous Coxsackie strain have been carried out with serum samples from all of the 6 patients excreting Coxsackie virus strains that produce myositis.

In the case of L.B., only one sample, taken 3 days after onset, was available; this contained no neutralizing antibody for the homologous virus. It will be seen that in the case of C.B. and M.T. there was a well marked increase in serum antibody levels, titres rising from zero in the acute phase to 1:300 or 1:500 in the convalescent. In the case of D.S. and A.P., antibody was already present in the samples removed 9 days after onset, and no difference was noted when

TABLE III.

RESULTS OF TESTING ACUTE AND CONVALESCENT PHASE SERA WITH HOMOLOGOUS VIRUS

Type of illness	*Patient yielding virus*	*Tests with patients' two phase sera and homologous virus*	
		Sera taken at following time after onset	*50% neutralizing titre*
Paralytic poliomyelitis	J.B.	(a) 11 days	0
		(b) 49 days	0
	D.S.	(a) 9 days	1:100
		(b) 45 days	1:100
	C.B.	(a) 3 days	0
		(b) 23 days	1:500
Non-paralytic poliomyelitis	A.P.	(a) 9 days	1:100
		(b) 36 days	1:100
	L.B.	(a) 3 days	0
	M.T.	(a) 1 day	0
		(b) 21 days	1:300

comparison was made with levels in samples removed in convalescence. No antibody to the homologous virus was found in the first or in the convalescent sample of J.B.

The results of the serological tests for recent mumps infection and infection with the virus of lymphocytic choriomeningitis were all negative.

DISCUSSION

This report describes the results of a study by clinical and laboratory methods of 22 patients admitted to the Hospital for Sick Children, Toronto, during the poliomyelitis season of 1950. In 21 of the patients a diagnosis of poliomyelitis of one or other of the usual varieties was made on clinical grounds. The remaining patient was suffering from an ascending type of paralysis of uncertain origin.

This study was carried out in the hope that it might be possible to make some clinical differentiation between Coxsackie and poliomyelitis infections, as well as to obtain some evidence regarding the incidence of Coxsackie illnesses simulating poliomyelitis.

No distinction could be made on clinical grounds between cases excreting and presumably infected with Coxsackie virus and those failing to excrete this agent.

With regard to the second object of the study, the relative prevalence of Coxsackie infections, strains of the virus were recovered from the stools of 8 patients of 22 studied. Six strains produced well marked myositis in 3-day old mice; 2 strains produced lesions in fat and brain. Tests for homologous antibody were carried out on the acute and convalescent phase sera of 5 of the 6 patients excreting myositis-producing strains. Antibody to the strain of virus isolated from the stool was found in the convalescent phase serum of 4 persons. In 2 of these a well marked rise in antibody level occurred in convalescence; homologous antibody was present in the acute phase serum (obtained 9 days after onset) of the other 2 patients, and did not increase in the later samples.

The serological results in the case of J.B., suffering from spinal paralysis, are of interest. No antibody to the homologous strain of virus was found in sera obtained 11 and 49 days after the onset of illness. It would appear, therefore, that J.B. excreted Coxsackie virus but did not develop antibody. This patient also excreted poliomyelitis virus and was presumably infected therewith.

It may be inferred from the results of the serological tests, that 4 of the patients excreting Coxsackie virus had definitely been infected therewith. One of these patients (D.S.) was suffering from spinal paralysis, one (C.B.) from bulbar poliomyelitis, and two (A.P. and M.T.) from the non-paralytic variety. D.S. and C.B. also excreted poliomyelitis virus, but the other two patients did not.

The eight strains of Coxsackie virus isolated are being studied with a view to investigating their relationship to similar strains isolated in the United States. These results are not yet complete, but it is probable that at least 4 types are represented in our collection of 8 strains.

In respect of the tests for the presence of poliomyelitis virus in stools, this agent was recovered from all 11 cases of paralytic poliomyelitis, but not from any of the same number of patients with the non-paralytic illness. This finding agrees with our results in previous years, and raises two possibilities: The first is that much less virus is excreted in the stool of cases of non-paralytic poliomyelitis than in the stool of cases of paralytic poliomyelitis. The second is that the syndrome of aseptic meningitis thought by clinicians to be caused by poliomyelitis virus is in fact only occasionally so caused. Of our 11 cases of aseptic meningitis diagnosed as suffering from non-paralytic poliomyelitis, Coxsackie virus was recovered from the stools of 5. No evidence concerning the etiology of the other 6 cases has been obtained.

In Table IV is presented a summary of the results of tests for the presence of poliomyelitis virus in the stools of cases of clinical poliomyelitis carried out during the past 2 years in our laboratory. Every test was made with ultracentrifuged extract and inoculations were given

TABLE IV.

RESULTS OF EXAMINATIONS OF STOOLS FOR PRESENCE OF POLIOMYELITIS VIRUS, TORONTO, 1949 AND 1950

Clinical diagnosis	*Number excreting poliomyelitis virus**
Bulbar or spinal poliomyelitis	16/17
Ascending paralysis	2/2
Non-paralytic poliomyelitis	1/14
Minor illness (abortive)	6/27

Total number of cases examined, 60.

*Ultracentrifuged extracts of stool; thalamic inoculation; all specimens collected within 2 weeks of onset.

thalamically. It will be seen that virus was recovered from the stools of 18 out of 19 persons with paralysis, 1 of 14 with non-paralytic poliomyelitis, and 6 of 27 with the abortive type of illness.

The question of the double excretion of poliomyelitis and Coxsackie viruses is of considerable interest. Both viruses were recovered from the stools of J.B. and D.S. suffering from paralytic poliomyelitis, and C.B. with the bulbar type of illness. The results of antibody tests suggested that D.S. and C.B. were infected with Coxsackie virus, but J.B. showed no serological evidence of infection.

During the past two years, we have isolated both viruses from single specimens of stool of 8 persons. As shown in Table V, one of these persons was a healthy contact, and the illnesses in the others ranged from a mild gastro-intestinal disorder to spinal or bulbar paralysis.

The significance of the double excretion of poliomyelitis and Coxsackie viruses is still in doubt. Probably it means only that the two infections have similar epidemiological characteristics.

It would seem reasonable to conclude from our observations, that in 1950 in Toronto a substantial number of all cases of poliomyelitis, paralytic or non-paralytic, were excreting Coxsackie virus. Many of those patients diagnosed as suffering from non-paralytic poliomyelitis were probably in fact infected with Coxsackie and not poliomyelitis virus.

TABLE V.

PATIENTS FROM WHOM BOTH POLIOMYELITIS AND COXSACKIE VIRUSES HAVE BEEN ISOLATED FROM STOOL SPECIMENS

Type of illness	*Initials of patient*	*Age (in years)*
Bulbar paralysis	C.B.	F., 7
Spinal paralysis	J.B.	F., 3
	D.S.	F., 2½
Ascending paralysis	L.Y.	M., 2
Aseptic meningitis (non-paralytic poliomyelitis)	A.O.	F., 6
Minor illness	B.J.	M., 2
Healthy family contact	Mr.J.	M., adult
Gastro-intestinal disorder	D.J.	M., 6/12

SUMMARY

1. This report describes a continuation of studies on the differentiation of poliomyelitis from poliomyelitis-like illnesses in Ontario.

2. In 1950, a detailed examination by clinical and laboratory methods was made of 22 children admitted to the Hospital for Sick Children, Toronto, with a clinical diagnosis of poliomyelitis.

3. Animal inoculation tests for the presence of Coxsackie and poliomyelitis viruses were performed on stool extracts prepared by ultracentrifugation.

4. In several patients proved to be excreting Coxsackie virus serological tests were carried out in suckling mice for the presence of homologous neutralizing antibody.

5. Ten children with typical paralytic poliomyelitis were studied: Poliomyelitis virus was recovered from the stools of all, and Coxsackie virus from the stools of 3 patients. These Coxsackie strains produced typical myositis in 3-day old mice.

6. Two of the patients with the spinal paralytic and one with the bulbar form of poliomyelitis excreted both poliomyelitis and Coxsackie viruses. This brings to a total of 8 the instances of double excretion reported from our laboratory.

7. One additional child suffering from an ascending paralysis of unknown etiology was found to be excreting poliomyelitis virus only.

8. Of 11 children with clinical non-paralytic poliomyelitis, none was excreting poliomyelitis virus in the stools. Five recoveries of Coxsackie virus were made from these patients; 3 of the strains produced myositis, and 2 caused lesions in fat and brain. The rarity with which poliomyelitis virus has been recovered from the stools of cases of clinically typical non-paralytic poliomyelitis in Toronto and vicinity is discussed.

9. Two-phase sera were available from 5 of the 6 patients excreting Coxsackie virus strains that caused myositis in mice. Homologous antibody was present in the serum of 4 of these patients, who may be assumed to have been infected with the agent isolated. The fifth patient failed to show any homologous Coxsackie antibody.

10. It is suggested that many cases of clinical poliomyelitis, mainly of the non-paralytic variety, that occurred in Toronto in 1950 were in fact infected with Coxsackie virus.

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REFERENCES

1. CURNEN, E. C., SHAW, E. W. AND MELNICK, J. L.: *J. A. M. A.*, 141: 894, 1949.
2. DALLDORF, G.: *Proc. New York State Assoc. P. H. Labs.*, 29: 54, 1949.

3. JAWORSKI, A. A. AND WEST, E. J.: *J. A. M. A.*, **141**: 902, 1949.
4. MELNICK, J. L., SHAW, E. W. AND CURNEN, E. C.: *Proc. Soc. Exper. Biol. & Med.*, **71**: 344, 1949.
5. SABIN, A. B. AND STEIGMAN, A. J.: *Am. J. Hyg.*, **49**: 176, 1949.
6. CHEEVER, F. S., DANIELS, J. B. AND HERSEY, E. F.: *J. Exper. Med.*, **92**: 153, 1950.
7. CURNEN, E. C.: *Bull. New York Acad. Med.*, **26**: 335, 1950.
8. HOWITT, B. F.: *Proc. Soc. Exper. Biol. & Med.*, **73**: 443, 1950.
9. MELNICK, J. L., LEDINKO, N., KAPLAN, A. S. AND KRAFT, L. M.: *J. Exper. Med.*, **91**: 185, 1950.
10. SLATER, E. A. AND SYVERTON, J. T.: *Proc. Soc. Exper. Biol. & Med.*, **74**: 509, 1950.
11. DALLDORF, G. AND SICKLES, G. M.: *Science*, **108**: 61, 1948.
12. DALLDORF, G., SICKLES, G. M., PLAGER, H. AND GIFFORD, R.: *J. Exper. Med.*, **89**: 567, 1949.
13. DALLDORF, G.: *Federation Proc.*, **9**: 569, 1950.
14. MELNICK, J. L. AND KAPLAN, A. S.: *Proc. Soc. Exper. Biol. & Med.*, **74**: 812, 1950.
15. ARMSTRONG, M. P., WILSON, F. H., MCLEAN, W. J., SILVERTHORNE, N., CLARK, E. M., RHODES, A. J., KNOWLES, D. S., RITCHIE, R. C. AND DONOHUE, W. L.: *Canad. J. Public Health*, **41**: 51, 1950.
16. RHODES, A. J., CLARK, E. M., KNOWLES, D. S., SHIMADA, F. T., RITCHIE, R. C., DONOHUE, W. L., ARMSTRONG, M. P., WILSON, F. H., MCLEAN, W. J. AND SILVERTHORNE, N.: *Canad. J. Pub. Health*, **41**: 183, 1950.
17. SILVERTHORNE, N., ARMSTRONG, M. P., GOODFELLOW, A. M., ROY, T. E., RITCHIE, R. C., DONOHUE, W. L., RHODES, A. J., CLARK, E. M., KNOWLES, D. S., SHIMADA, F. T. AND WILSON, F. H.: *Canad. M. A. J.*, **64**: 309, 1951.
18. SILVERTHORNE, N., GOODFELLOW, A. M., ANGLIN, C., RHODES, A. J., ROY, T. E. AND SNELLING, C. E.: *Canad. M. A. J.*, **60**: 356, 1949.
19. SILVERTHORNE, N., ARMSTRONG, M. P., WILSON, F. H., DONOHUE, W. L., GOODFELLOW, A. M., ROY, T. E., MCCLELLAND, L., CLARK, E. M. AND RHODES, A. J.: *Canad. M. A. J.*, **61**: 241, 1949.
20. RHODES, A. J., MCCLELLAND, L. AND DONOHUE, W. L.: *Canad. M. A. J.*, **60**: 359, 1949.
21. CLARK, E. M., KNOWLES, D. S., SHIMADA, F. T., RHODES, A. J., RITCHIE, R. C. AND DONOHUE, W. L.: *Canad. J. Pub. Health*, **42**: 103, 1951.
22. PAPPENHEIMER, A. M., DANIELS, J. B., CHEEVER, F. S. AND WELLER, T. H.: *J. Exper. Med.*, **92**: 169, 1950.
23. SICKLES, G. M. AND DALLDORF, G.: *Proc. Soc. Exper. Biol. & Med.*, **72**: 30, 1949.
24. MELNICK, J. L. AND LEDINKO, N.: *J. Exper. Med.*, **92**: 463, 1950.

THE DECLINE OF ARTIFICIAL PNEUMOTHORAX*

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THERAPEUTIC ARTIFICIAL PNEUMOTHORAX in pulmonary tuberculosis is a procedure which has undergone a long test. It was in 1892 that Forlanini introduced it as a method of treatment[1] although it was mentioned earlier and was even attempted. For a chronic disease of so protean a nature as tuberculosis, there is a strong tendency to perpetuate any therapeutic measure which has, in some cases, contributed to cure. During the nineteen twenties and later, artificial pneumothorax gained such popularity that it almost superseded the time-honoured principle of rest.[2] Unfortunately, unlike some other innovations in treatment, the efficacy of pneumothorax has not been scientifically assessed, since a completely controlled series with the elimination of all extraneous variables, presents a problem well nigh impossible of solution.

At the Toronto Hospital for Tuberculosis, Weston, the years of peak usage were within the past decade, actually 1942-43. At that time surgical collapse and pulmonary resection were not as widely, nor as safely, employed as now, artificial pneumoperitoneum was not used,[3] and antibiotics were not available.

Since the peak period of use of pneumothorax, its popularity has shown a marked decline at this hospital. This trend has paralleled that of many of the other larger treatment centres. The question is, therefore, whether experience in sanatoria equipped to carry out the necessary surgical procedures justifies a gradual or even rapid abandonment of this debatable method of treatment. This survey is merely another attempt to provide the answer. It is actually a follow-up of cases, at least five and mostly eight years after induction with a view to ascertaining the frequency and severity of complications and to note the eventual outcome of cases so treated. It has been necessary to tabulate many results, because generalizations alone would defeat the purpose of this study. However, figures are reduced to a reasonable minimum, and emphasis is given to their interpretation. Assessments are made in terms of (a) initial collapse, satisfactory or otherwise; (b) results of pneumothorax after re-expansion; and (c) final outcome of treatment as gauged by present condition of patient.

Satisfactory collapse is accepted when anatomically efficient pneumothorax is initially obtained, where necessary by closed intrapleural pneumonolysis, and free from immediate complications. This conclusion can be reached following complete or attempted pneumonolysis, where interfering adhesions are present.

Results of pneumothorax treatment are measured in terms of good, fair and poor. These estimations are, naturally, exclusive of unsuccessfully attempted pneumothoraces due to pleural symphisis. The results are termed good where the object for which pneumothorax is induced is attained without major complications. If such should arise they must not appreciably affect the results of therapy. The category of fair is ap-

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plied when complications or inadequate collapse may affect the efficacy of treatment but the purpose for which pneumothorax was employed is eventually attained, even at a rather excessive price. The results are termed poor where inadequacy of collapse or developing complications defeat the purpose for which pneumothorax was initiated, including some instances where results of therapy were worse than might be expected if pneumothorax had never been induced. In this group are included those pneumos which were entirely unsatisfactory and had to be terminated at an early date. Their purpose was not accomplished. Results are poor where the treated lung becomes re-activated or excavated shortly after re-expansion. This good, fair, poor assessment is necessarily measured with a rather arbitrary rule, but an attempt is made at consistence and fairness. Various authorities will differ somewhat in the allocation of pneumo cases as good or poor. There are members of our staff who would reduce the number of cases in this series which have been reported as good. However, it is my belief that the method of assessment adopted is fair.

Although appearing further to complicate the evaluation of results of pneumothorax, it has become necessary to draw a line between results of pneumothorax therapy and final outcome of sanatorium treatment. The correlation generally runs high. If the results of pneumo are good it usually follows that the eventual outcome, in any given case, will be satisfactory. However, there are a number of exceptions where this specific therapy may be highly satisfactory in the handling of lesions on one side, while the condition of the patient may be deteriorating from extending contralateral disease. Conversely, in many instances the results of pneumothorax may be disappointing and yet thanks to substitute therapy or specific resistance of the patient, the disease becomes arrested. This evaluation is measured in terms of clinical status as standardized by the National Tuberculosis Association in follow-up of the patients.

The total number of cases presented is 295 with 374 attempted pneumos. Of this number 24 cases with 32 pneumos could not be traced and therefore do not contribute to the final assessment. Thus in the follow-up study the number of cases is reduced to 271 with 342 attempted pneumos. This is primarily an unselected group of cases whose pneumothorax or pneumothoraces were induced in the years 1941 through 1945. By far the largest number were induced in 1942-43, namely, 241 of the total of 374.

Of 342 pneumos a definite history and/or radiological evidence of former pleurisy was recorded in 61 instances. In 18% initial satisfactory collapse was obtained, and the results of pneumothorax treatment were: good, 4.9%; fair, 3.3%; poor, 54.1%; not induced, 37.7%. These results contrast with those of the group of 281 in which no former indication of pleurisy could be obtained. Satisfactory collapse was obtained in 30.6%, and good were 15.7%; fair, 14.2%; poor, 53.4%; and not induced 16.7%.

With regard to type of disease, as indicated radiologically, 164 were exudative, 170 mixed disease, 7 productive and 1 tuberculoma. Satisfactory collapse was obtained in 39.0% of exudatives and only in 18.8% of pneumos attempted in mixed disease. Only 14.0% were not induced of the exudative group, but 25.3% of mixed showed pleural symphisis. The ratio of good, fair and poor was not startingly dissimilar.

At least one definite cavity was diagnosed radiologically in 217 instances, often, in more recent years, with the assistance of planography. Results were; good, 9.2%; fair, 11.5%; poor, 55.3%; and not induced 24.0%. In the small group of 31, in which cavitation was suggested rather than established, the findings did not appreciably differ, excepting that a slightly higher percentage of good results was recorded. In those pneumos performed in the absence of recognizable excavation, results were; good, 21.3%; fair, 17.0%; poor, 46.8%; and not induced 14.9%.

Table I is a breakdown of results of pneumo with relation to interval between diagnosis of pulmonary tuberculosis and commencement of pneumothorax.

TABLE I.

Interval between diagnosis and induction in months	*Number of pneumos in each group*	*Attempted but not induced %*	*Good %*	*Fair %*	*Poor %*
0 - 1	83	21.7	16.9	10.8	50.6
2 - 5	142	19.7	12.7	14.1	53.5
6 - 11	43	25.6	9.3	16.3	48.8
12 - 23	25	12.0	12.0	4.0	72.0
24+	49	22.5	16.3	10.2	51.0

Table II is an expression of the type and extent of disease. The findings are approximately comparable to those of other investigators.

TABLE II.

Extent of disease	*Number of pneumos in each group*	*Number with initially satisfactory collapse*	*Attempted but not induced* %	*Good* %	*Fair* %	*Poor* %
Minimal	25	18	8.0	40.0	12.0	40.0
Moderately advanced	162	55	16.1	17.3	14.8	51.8
Far advanced	153	28	27.4	5.2	9.8	57.6
Primary type	2	1	50.0	50.0		

Table III shows a breakdown of disease by location as to upper, middle or lower thirds of lung, as noted on P.A. chest films.

In Table IV, in terms of the final outcome of treatment, a contrast is drawn between contralateral pneumo cases and unilateral cases. Also cases of contralateral disease where only unilateral pneumothorax treatment was employed are compared with pneumo cases with strictly unilateral disease. Those attempted but not induced are compared with those in which induction was possible. Comparison of satisfactory with unsatisfactory pneumos is made and expressed in terms of final outcome of treatment. These results are measured in terms of patients rather than lungs.

Table V demonstrates the frequency of complications in 342 pneumos. In many instances more than one was present. In 288, interfering adhesions were present. This figure includes 71 attempted but not induced pneumos, because of pleural symphisis. In another 4 pneumos adhesions were present but not interfering. As indicated at bottom of the table, in 59 pneumonolysis was complete, and in 28, complete severance of all adhesions was not feasible. Most of the remainder were thoracoscoped but severance of adhesions was either not possible or not indicated as in cases of acute pleuritis or in the findings of numerous pleural tubercles.

A further breakdown of cases as to eventual outcome and duration of treatment is illuminat-

TABLE III.

Location of disease in thirds of lung	*Number of pneumos in each group*	*Attempted but not induced* %	*Good* %	*Fair* %	*Poor* %
Apex only	38	13.1	26.3	5.3	55.3
Upper	132	20.5	14.4	15.9	49.2
Upper and middle	94	24.5	7.4	9.6	58.5
Upper, middle and lower	47	25.6	2.1	12.8	59.5
Middle	13	7.7	38.5	23.1	37.7
Lower	6	16.7	33.3	0	50.0
Middle and lower	12	16.7	25.0	8.3	50.0
Upper and lower	0				

TABLE IV.

Eventual outcome of treatment	*Number of cases*	*Number now empl'd.*	*Appar. cured* %	*Arres.* %	*Appar. arres.* %	*Quiescent* %	*Active* %	*Died* %
Bilateral pneumos	71	31	38.0	14.1	1.4	1.4	15.5	29.6
Unilateral pneumos	200	112	50.0	9.5	1.5	3.5	4.0	31.5
Bilateral disease with unilateral pneumo	111	52	41.4	8.2	2.7	3.6	2.7	41.4
Unilateral disease with pneumo	89	60	60.7	11.2	0	3.4	5.6	19.1
Unsuccessfully attempted	54	27	40.7	16.7	0	1.9	3.7	37.0
Successfully induced pneumos	217	116	48.4	9.2	1.8	3.2	7.9	29.5
Initially satisfactory pneumos	76	54	63.1	17.1	5.3	1.3	7.9	5.3
Unsatisfactory pneumos	195	90	40.0	8.2	0.5	3.6	6.7	41.0

TABLE V.

Incidence of complications in 271 induced pneumos	*Total number*	*Good %*	*Fair %*	*Poor %*
Adhesions interfering excluding not induced—71	217	14.3	13.4	72.3
Pleural tubercles or pleuritis	39	20.5	10.3	69.2
Definite atelectasis	77	7.8	16.9	75.3
Uncollapsed cavity	89	1.1	4.5	94.4
Repeated spontaneous pneumothorax	14	14.3	14.3	71.4
Transient effusion	67	26.9	20.9	52.2
Persistent non-tuberculous effusion	30	23.3	33.3	43.4
Persistent tuberculous effusion	39	0	7.7	92.3
Obliterative pleuritis	51	35.3	25.5	39.2
Residual pleural thickening	83	15.7	30.1	54.2
Gross diaphragmatic adhesions	29	24.2	37.9	37.9
Inexpandable lung	24	0	41.7	58.3
Complete pneumonolysis	59	42.4	25.4	32.2
Incomplete pneumonolysis	28	10.7	25.0	64.3

ing. Eighty-four patients died, representing 105 pneumos. Of this number, 27 were not induced. Of the 84 patients, pneumothorax was abandoned in 57, and carried to the end in 27. In patients living 45 attempts were not successful. From the total of 342 the substraction of 45 and 105 leaves 192. Of this number 28 are still receiving refills, in almost all instances because of inexpandable lung. Of the remaining 164, (A) 47 were discontinued having served their purpose, and (B) 117 were necessarily discontinued before purpose was attained because of unsatisfactory collapse or severe complications. In group (A) pneumothorax was carried for an average of 54.2 months, and in group (B) for 9.5 months. Average period in months from discontinuance of pneumothorax to assessment was 26.9 in group (A) and 63.7 in group (B).

DISCUSSION

In considering the findings of this study further reference is made to the foregoing tables. It is appreciated that the deductions offered are not unequivocal and that in many instances somewhat divergent interpretations might be possible.

In noting type and extent of disease, mixed disease is taken as that type of lesion the radiological appearance of which includes more than a fluffy exudative infiltration. Linear and circumscribed densities are also present. Although it is generally recognized that little indication for artificial pneumothorax exists in purely productive disease, the results in mixed lesions are almost comparable to those in exudative. However, satisfactory collapse was obtained twice as frequently in exudative lesions.

The results were considerably better in cases without obvious cavitation. It must be considered that excavated lungs often demonstrate more extensive involvement than those showing no evidence of cavity. Satisfactory collapse is attained twice as often in the non-cavitary disease; and nearly double the percentage of good and fair results were obtained. Of the 217 cases with cavitation, 89 were not collapsed by artificial pneumothorax. This constitutes a failure rate of 41% when the procedure is employed primarily for this purpose. This is particularly disappointing when it is realized that most cases with large tension cavities were excluded from this series, for it was appreciated even during the period of peak enthusiasm, that in their treatment pneumothorax had little to offer.[4]

Table I indicates that results are not inversely proportional to the haste with which pneumothorax is begun following diagnosis. The figures are not startlingly dissimilar when any period up to and even beyond two years after discovery of pulmonary tuberculosis is selected as the preferable time to commence pneumothorax treatment. It can be appreciated that in many cases it is expedient to delay, particularly in the presence of tension cavities, acute endobronchial disease, and in pneumonic lesions. It might be suggested that, by and large, a period of observation is indicated in cases in which pneumothorax is being contemplated. Some complications can thus be reduced and some cases might be weeded out for primary treatment with other more suitable and definitive therapeutic measures.

Comparing cases with definite history or radiological evidence of former pleurisy on the

side selected for pneumothorax collapse against those with no such evidence suggests that the procedure is hardly worth attempting where pleural inflammation has antedated parenchymal infiltration.

With regard to type and extent of disease, there is rarely indication for use of pneumothorax in primary type disease, perhaps only in an attempt to close small cavities and certainly not in the treatment of pneumonic or atelectatic lungs. As has been frequently recognized, Table II shows that favourable results vary inversely as the extent of the lesion. Thus the best results may be obtained in the treatment of minimal disease. However, it has been established that a large percentage of minimal cases respond well to bed rest alone, without exposure to the risks of pneumothorax. The results in far advanced disease are poor. It is in this group that one might hope for assistance, but from this procedure, it is evidently not forthcoming: 57% gave poor results, and this figure is exclusive of those not successfully induced.

The breakdown of cases with relation to location of lesions, shows best results when only one-third of the lung demonstrates disease. If such is situated in the middle third, results are better than in the upper or lower thirds.[5] Least favourable results were obtained in the upper third infiltration. Where disease was restricted to apex results were disappointing on consideration of the small area involved. These findings are interesting; and it is regrettable that, because of breakdown, the number presented is small.

Table IV shows the final outcome of treatment, necessarily in terms of patients rather than pneumos. While it has already been demonstrated that long term results of artificial pneumothorax are not good, the final picture was only slightly worse for the bilaterally-treated cases. It should be taken into consideration that many of the unilateral-treated cases showed contralateral disease, but, of course, all of the bilaterals had involvement of both lungs. In a further breakdown, cases of contralateral disease with only one side treated by pneumothorax are compared with unilateral disease so treated, and the results are considerably better in the latter group. Considering the attempted but not induced in contrast to the successfully induced, the final outcome proves interesting, in that the results are almost alike. Granted that other lesser factors may play a part, it would seem reasonable to interpret these findings as indicative that the ill effects of pneumothorax approximately cancelled the favourable effects so that the final outcome was not appreciably altered by its use. If such an interpretation is logical, at least in this group of cases, one might ask wherein lies the contribution of artificial pneumothorax.

The group of pneumos in which satisfactory collapse was obtained is compared with those which were unsatisfactory. In the latter group fall those whose induction was not possible because of the absence of a free pleural space. Results are shown in terms of final outcome of cases. In the results of pneumothorax a striking contrast is herein evidenced.[6] It would appear relevant to draw attention to a large series of cases presented by Jennings, Mattill and Nemec[7] where the fatality rate for patients in whom pneumothorax was unsatisfactory was approximately 25% higher than for those in whom no pleural space was found. This prognosis was considerably worsened by the use of pneumothorax; and in reviewing patients after re-expansion of pneumothorax, it has been pointed out that the eventual prognosis was dependent more on whether the collapse was anatomically satisfactory than on any other factor. Therefore, unless collapse is effective, or can be promptly rendered so by pneumonolysis, it should be abandoned without delay.

In my opinion those cases which at the present time might at least be considered eligible for treatment by pneumothorax are contrasted with those which could not now be accepted for this type of treatment in light of present opinion at this hospital. The results are decidedly better for the former group of 125 against 217 which would now be otherwise treated. Satisfactory collapse was obtained in 46.6% of the first group and good results of pneumothorax in 26.4% against figures of 14.3% and 6.5% in the would-not-be-attempted group. This indicates that our present conservative attitude is a step in the right direction. The suggested question is whether results might not be further improved by a greater reduction in the pneumothorax-treated cases.

Complications of artificial pneumothorax are fortunately not always serious, but they are at least frequent and numerous. In keeping with early unsatisfactory collapse, the appearance of certain complications calls for cessation of this form of treatment. This holds for acute pleuritis, with or without evident tubercles, persistent effusion, tuberculous or otherwise, and uncollapsed

cavities following adequate trial of therapy.[8] A large percentage of persistent sizeable effusions are tuberculous on culture if proper methods are employed, and they, therefore, constitute potential empyemata if re-expansion is not brought about promptly[9, 10] With view to further reducing complications, at this centre routine pre-collapse bronchoscopic examination has been in effect since 1945. Through this precaution the acute œdematous or stenosing bronchitis cases are eliminated. These formerly contributed to a large number of atelectatic lungs or segments of lungs following induction.[8] Now, at the Toronto Hospital for Tuberculosis, artificial pneumothorax might be considered only in the treatment of (a) mid-lung disease, (b) diffusely scattered unilateral exudative disease, which is not, or which might not be expected to be, adequately handled by non-collapse measures, and (c) on rare occasions in the unilateral treatment of bilateral disease, in preparation for surgical collapse or resection of the contralateral lung.

It would appear that combined treatment with streptomycin and pneumothorax may improve the results of the latter, and substantially reduce its risks.[11] A relatively small number of cases so treated at this hospital, to date, have run into fewer complications than those presented in this series. However, the period has been too short and the number too small for statistical assessment at this time.

With the findings of this paper in mind, I would like to suggest a theoretical case for which pneumothorax might be the treatment of choice. This patient should give no history of former pleurisy on the side in question. The disease should be unilateral, exudative, mid lung in position, involving less than one-third of the field, and after an adequate period of observation, and treatment if indicated, by non-collapse methods, fails to respond or actually extends. If cavitation is present it should not be extensive. Acute or stenosing endobronchial disease should be excluded by pre-pneumo bronchoscopy. If adhesions are present they should lend themselves to complete pneumonolysis. Such prerequisites would reduce the number of cases for which pneumothorax would appear indicated to a small number of the admissions to the average sanatorium.

CONCLUSIONS

A detailed statistical analysis of cases of pulmonary tuberculosis treated by artificial pneumothorax is presented in the foregoing paragraphs. The results are not good. Of 342 instances in which pneumothorax was attempted, only 47 or 13.7% were eventually discontinued with their purpose having been served. This low figure is higher than those of some other investigators;[12] but an inescapable conclusion presents, namely, that this procedure surely would have long since been discarded had a less drastic, more satisfactory method of treatment appeared. The slow acceptance of substitute therapy has permitted the wide use, for a long period, of a therapeutic measure whose results are poor in a large percentage of cases.

SUMMARY

A follow-up survey of cases of pulmonary tuberculosis, treated by artificial pneumothorax, is presented.

In 295 patients, 374 pneumothoraces were studied. Of these, 24 patients, with 32 pneumos, could not be traced, reducing the number with complete follow-up to 271 patients with 342 pneumos: 64% were induced in 1942-43.

Assessments were made in terms of: (a) initial collapse, satisfactory or otherwise, (b) results of pneumothorax after re-expansion, and (c) final outcome of treatment as gauged by present condition of patient.

Effects of treatment on type, extent and site of disease, are recorded, as well as the relation of various complications to the final outcome.

The overall results are poor; and it is suggested that the use of artificial pneumothorax in the treatment of pulmonary tuberculosis be substantially reduced.

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Appreciation is likewise extended to the staffs of the medical record library and radiology department for their material assistance.

REFERENCES

1. PACKARD, E. N., HAYES, J. N. AND BLANCHET, S. F.: Artificial Pneumothorax, Lea and Febiger, Philadelphia, 1940.
2. HAYES, J. N.: *Am. Rev. Tuberc.*, **62**: 90, 1950.
3. TRIMBLE, H. G., EATON, J. L., CRENSHAW, G. L. AND GOURLEY, I.: *Am. Rev. Tuberc.*, **57**: 433, 1948.
4. SWAINE, C.: *M. J. Australia*, **2**: 658, 1947.
5. ROTHSTEIN, E.: *Am. Rev. Tuberc.*, **59**: 50, 1949.
6. LIVINGSTONE, J. L.: *J. Roy. Inst. Public Health & Hyg.*, **2**: 579, 1939.
7. JENNINGS, F. L., MATTILL, P. M. AND NEMEC, F. C.: *Am. Rev. Tuberc.*, **42**: 431, 1940.
8. RAFFERTY, T. N.: Artificial Pneumothorax in Pulmonary Tuberculosis, Grune and Stratton, New York, 1945.
9. CLARK, G. L.: *New Zealand M. J.*, **46**: 331, 1947.
10. MORRISON, J. B.: *Am. Rev. Tuberc.*, **57**: 598, 1948.
11. HYMAN, G. A. AND HOFFMAN, S. H.: **59**: 539, 1949.
12. HURST, A. AND SCHWARTZ, S.: *Am. Rev. Tuberc.*, **45**: 132, 1942.

LEUKÆMIA IN CHILDREN

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AS A CONSEQUENCE of reports by Farber and his associates[1, 2] concerning temporary remissions in the acute leukæmias of children produced by folic acid antagonists, it was decided to determine the effect of these chemicals in a series of leukæmia patients at the Hospital for Sick Children. The results of this method of treatment will be reported in the following communication. As an adjuvant in the appraisal of the use of the folic acid antagonists in the treatment of leukæmia in children, it was considered advisable to review some of the previous experiences in this disease. The purpose of this paper is to present briefly the results of this survey.

During a 16-year period, from January, 1932 to December, 1947, 158 cases of leukæmia under 14 years of age, were admitted. In this interval, there was a total of 145,799 indoor admissions to the hospital, giving an over-all incidence for leukæmia of 0.1%.

Age at onset of illness.—The youngest patient in which a diagnosis of leukæmia was made was eight weeks old. This was one of eight cases occurring under one year. Over one year of age, there was a steep rise in the number of cases to the age of 4 years, with a gradual fall thereafter to 14 years (Fig. 1). The average age at which symptoms first commenced was 4 years, 11 months.

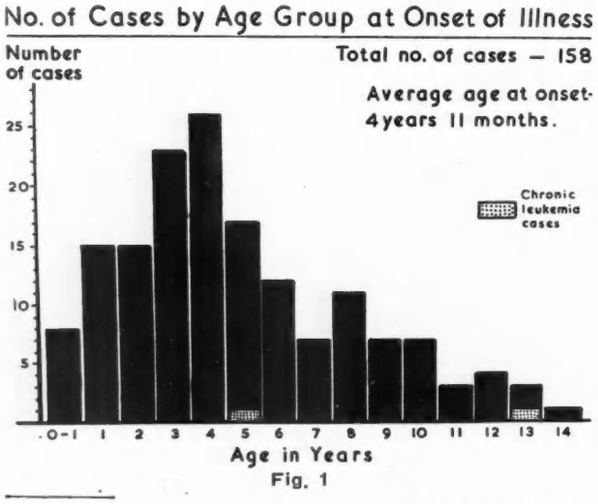

Fig. 1

*From the Laboratories of The Hospital for Sick Children and the Department of Pathology, the University of Toronto.
†From the wards of The Hospital for Sick Children and the Department of Pædiatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P.(Lond.).

Sex incidence.—62.7% of the cases occurred in males, giving a preponderance in the male sex, a finding that has been noted by others.[3, 8, 9]

Race, environment and economic status.—There was no detectable relationship between the occurrence of leukæmia and any race, environment or economic status.

Initial symptoms on admission.—The complaints most often recorded on admission to the hospital were non-specific, being those that are frequently associated with a number of diseases. These included pallor, loss of appetite, malaise, fatigue, weakness and fever (Fig. 2). Less frequent but more diagnostic symptoms included generalized or localized lymph gland enlargement, manifestations of a hæmorrhagic tendency, loss of weight, and bone and joint complaints. It is interesting to note that there were 29 cases in which there were bone and/or joint symptoms. The majority of these were initially diagnosed as either rheumatoid arthritis or rheumatic fever, and later, as the disease progressed, were correctly labelled as leukæmia.

Occasional complaints were abdominal pain, the presence of a tumour mass, and stomatitis. The abdominal pain was vague, indefinite, not localized and probably due to interference with the normal function of the gut, or stretching of the attachments of an enlarged liver or spleen. In regard to the presence of a tumour mass, 11 cases were brought to the physician because of the discovery of a large palpable mass in the abdomen. In all of these cases, the mass was found to be an enlarged spleen. In only three patients in the series was stomatitis recorded as occurring in any stage of the disease. This is of interest because in adults it is not infrequently an initial feature, particularly in the monocytic type of leukæmia.

Physical examination.—Records of the physical examination were available on 153 patients (Fig. 3). Of these, there was lymph gland enlargement in 126, splenomegaly in 126, hepatomegaly in 114, and hæmorrhagic manifestation in 82. These findings are in accord with the usual descriptions in the standard pædiatric texts.[4, 5]

LABORATORY FINDINGS

Red blood cells and hæmoglobin.—Initial hæmoglobin values ranged from 2 gm. to 13 gm. %. 102 of the patients had an anæmia on admission (less than 10.0 gm. %) which, in all cases was treated by transfusion. The other 56

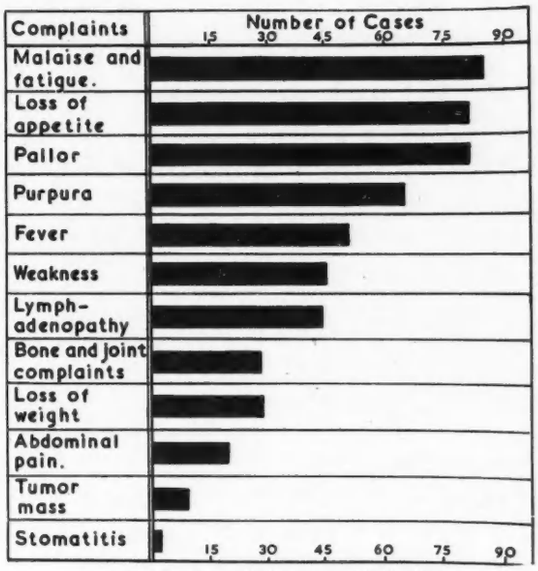

Fig. 2.—Complaints on admission. Total number of cases—158.

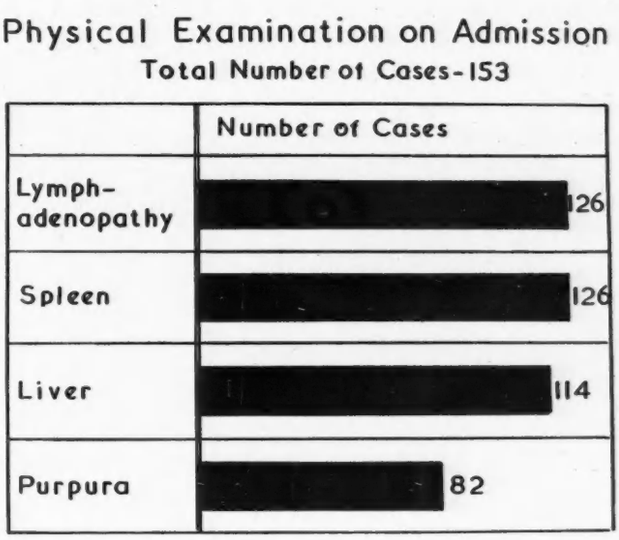

Fig. 3

developed varying degrees of anæmia as their disease progressed. In those cases which received palliative transfusion, the hæmoglobin was raised only temporarily. There was no indication that direct transfusions were of more benefit than indirect (bank blood).

White blood cells.—The admission white blood counts varied between 1,000 and 1,250,000/c.mm. Thirty-eight of 155 patients, in which the white counts were recorded, showed an aleukæmic picture throughout the illness, the counts not exceeding 10,000 at any time. All of these cases were diagnosed as lymphatic leukæmia, except one which was called acute granulocytic leukæmia. It is noteworthy that although the total white count was within normal limits, 34 of these cases had leukæmic "blast" cells in the peripheral films. Of the 4 with no abnormal forms in the peripheral blood, 3 had typical leukæmic bone marrow films and in one the diagnosis was established only by post-mortem examination. The average duration of these aleukæmic cases was 4.8 months. An additional 45 cases had white counts that fell below 10,000 at some stage of their illness. There were 21 patients whose white counts at no time went below 100,000. The average duration of illness in these cases was 2.2 months.

Platelets.—In 128 patients, the platelets were either described from smears or recorded as platelet counts. In 111 of these, the platelets were definitely decreased.

Sternal marrows.—Of 33 marrow punctures carried out in the latter years of the series, 26 were definitely positive and 9 were "indefinite". Relatively few marrow examinations were made prior to the second World War. During the war years much of this work was delegated, of necessity, to untrained personnel. This probably accounts for the high proportion of "indefinite" marrow films in established cases of leukæmia.

X-rays.—X-rays of the long bones were taken in 38 cases. Of these, 18 showed definite abnormalities, such as periosteal elevation and a zone of rarefaction at the diaphyseal side of the epiphyseal plate of the long bones, which have been reported as indicative of leukæmia.[6, 7]

DIAGNOSIS

The final diagnosis of leukæmia was established on the basis of peripheral blood findings, sternal marrow punctures, biopsy, and autopsy, either singly or in combination. In the 158 cases, the following diagnoses were made: acute lymphatic, 133; acute granulocytic, 10; acute leukæmia, unspecific, 7; acute monocytic, 6; chronic granulocytic, 2.

The diagnosis of a specific type of acute leukæmia was made in all but 7 of the above cases. However, at the present time, we feel that an attempt to classify a case of leukæmia in a child as to the origin of the leukæmic cells is specious, unless there is unequivocal evidence that it belongs to one of the various types. In most cases the leukæmic cell or "blast" is so undifferentiated that an accurate determination of its probable origin is impossible. The majority

of cases are simply designated "acute leukæmia". Usually when the initial diagnosis is made, it is not possible to predict the probable duration of the disease, except within wide limits. Hence, a classification of the disease as to its acuteness or chronicity can be made best in retrospect. Arbitrarily, we group into the "acute leukæmias" those whose total duration of illness is less than 9 months, into the "subacute" those who live from 9 months to 2 years, and into the "chronic" those who survive over two years from the onset of their illness. In all but 6 of the 158 cases, the date of death is known and on the basis of our present conception, this series may be reclassified as follows: acute leukæmia, 139; subacute leukæmia, 11; chronic granulocytic leukæmia, 2.

Post mortem examinations. – Autopsies were performed on 45 of the patients. All except one showed typical leukæmic infiltrations in many organs. The exception was a case that had been treated with radio-active phosphorus, following which there was a dramatic drop in white blood count. Death resulted shortly thereafter. Post mortem examination revealed hypoplasia of the bone marrow with scanty foci of leukæmic cells and minor degrees of leukæmic infiltration elsewhere in the body.

TREATMENT

A. *Radiation.* (1) *X-ray therapy.*—There were 12 patients in this series treated by radiation. Of these, there were 9 acute, 2 subacute, and 1 chronic granulocytic. There was specific indication for radiation in only one child, in which enlarged mediastinal glands were obstructing respiration by pressure on the trachea. As the average duration of illness in the 9 acute cases was 4.2 months, it is obvious that this form of treatment had little effect on the course of the disease. In the two subacute cases which survived 10 and 13 months from the onset of symptoms, it was not considered that radiation materially prolonged life, as in each case the treatment was not given until one month prior to death. The one chronic case who received radiotherapy was a typical granulocytic leukæmia who received repeated radiation to the spleen. He survived 53 months. In view of the fact that the only other chronic leukæmia in our series lived for 50 months and had no specific form of therapy, it is doubtful if radiation had much effect on the duration of the disease. Initial radiation had the effect of reducing the white blood counts and decreasing the size of the enlarged glands, liver and spleen. However, it was noted that further courses proved to be less effective. Radiation did not appear to hasten death except possibly in two cases. In each of these, the radiation that was administered lowered the white counts below 800 and the patients died a few days after the termination of therapy.

(2) *Radio-active isotopes.*—Two patients were treated with radio-active phosphorus. One with a white count of 200,000 was given 15 c.c. of a solution of radio-active phosphorus (2.3 millicuries of radio-phosphorus in 65 mgm. Na_2HPO_4) by gavage; 18 days later he died with a terminal total white count of 24 cells. At no time was there any evidence of clinical improvement, although at post mortem there was extensive destruction of leukæmic cells. The other case was given 1 c.c. of the radio-active phosphorus solution by mouth twice a day for 4 days. Death occurred five days after the termination of the treatment. There was no appreciable effect either clinically or hæmatologically. No post mortem was obtained.

B. *Urethane.*—There was 1 case of acute leukæmia treated with urethane, the duration of illness being 4 months. No effect was achieved from the use of the drug.

C. *Pentnucleotide.* – Eleven patients were treated with pentnucleotide. In only one of these was there any effect that might be attributed to the therapy, that being a case in which there was a fall in white count from 14,000 to 400 in 8 days with death occurring two days later.

One of the cases which is included in the group of subacute leukæmias was treated with pentnucleotide. The duration of illness was 16 months. However, in analyzing the clinical course and the blood findings, it is not considered that this form of therapy was responsible for the subacute course of the disease.

D. *Transfusion.* – 124 cases received either direct or indirect transfusions as a palliative method of therapy. There is little doubt that this, as a temporary measure, was the most effective type of treatment. In no case was an exsanguination or exchange method of transportation performed.

Duration and progress of illness.—Of the 158 cases, 6 could not be traced, but the date of death was ascertained in 152 (Fig. 4). The average total duration of illness of these 152, from the onset of symptoms until death, was 4.2 months.

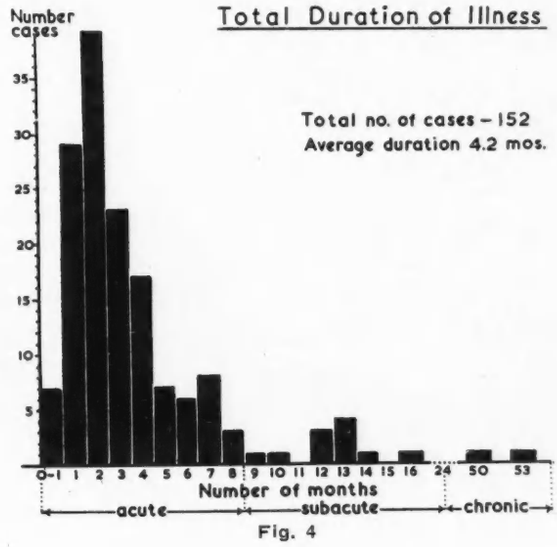

Fig. 4

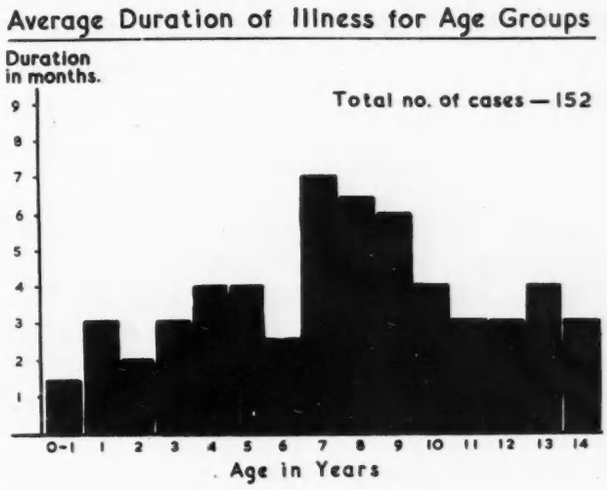

Fig. 5

139 cases died within 9 months from the onset of symptoms; these we have arbitrarily designated as acute leukæmia. The average duration in this group was 2.9 months.

There were 11 so-called subacute cases who survived between 9 and 24 months with an average duration of 12.4 months. The average age at onset of this group was 6.3 years, which is somewhat older than the average for leukæmia in children. Of these 11 cases, 8 were aleukæmic, 7 remaining so throughout the illness and one becoming a typical fulminating case with high white blood counts terminally. The other 3 cases had initial high white counts which fell below 10,000 as the disease progressed. Symptomatic treatment only was used in 8 cases. Two children had radiation therapy and one was treated with sodium pentnucleotide, neither of these procedures apparently having any effect on the course of the disease. These 11 "subacute" leukæmias, whose total duration of illness was somewhere between 9 and 16 months, indicate that caution is necessary in evaluating the usefulness of a new form of therapy, as regards prolongation of life. In general it appears that even though the leukæmic cell is undifferentiated, if the patient persists in a more or less aleukæmic phase, there is more likelihood of a longer survival time than if the patient has a high white count.

In these series, two cases were diagnosed as chronic granulocytic leukæmia. One of these, a boy 13 years old at the onset of his disease, was typical in regard to clinical picture, hæmatological findings and subsequent course. He was treated by repeated radiation to the spleen and survived 53 months. The other, a 5 year old male, was initially labelled as an undiagnosed anæmia with splenomegaly. A splenectomy was performed and the histological diagnosis was probable leukæmia. Later, a typical leukæmic blood picture developed and on the basis of the cytological appearance of the abnormal cells, a diagnosis of monocytic leukæmia was made. Based on post mortem findings, the final diagnosis was an eosinophilic variation of a granulocytic leukæmia. In retrospect, it is believed that the cells that were thought to be monocytes were probably eosinophils devoid of granules, if such a paradox can be granted. No radiotherapy was given. The child survived for 50 months from onset of symptoms.

The average length of illness for each age group was calculated (Fig. 5). There was a gradual rise in duration from under 1 year to 7, 8 and 9 years of age, and then a gradual fall to 14 years of age. Thus, those whose symptoms begin at the age of 7, 8 or 9, have a slightly longer expectancy of life than those in whom symptoms develop at a younger or an older age.

In no case in this series was there any record of a clear-cut remission that was either spontaneous or subsequent to an infection.

SUMMARY

1. The history of 148 cases of leukæmia in children prior to treatment with the folic acid antagonists has been reviewed.

2. Over 90% of the patients in this series had the acute fulminating type of leukæmia with an average duration of life from the onset of symptoms of less than three months.

3. Approximately 7% of the cases were classified as "subacute" with an average survival of more than 12 months. In the appraisal of any new form of therapy, this group must be kept in mind.

4. Chronic granulocytic leukæmia in children is rare. In this series, no case was encountered in which a diagnosis of chronic lymphatic leukæmia was made.

5. In the group of patients under consideration, there was no indication that the types of therapy employed had any beneficial effect in regard to the prolongation of life.

REFERENCES

1. FARBER, S.: *Proc. Div. Laboratories & Research*, 1: 1, 1948.
2. FARBER, S. AND DIAMOND, L. K. *et al.*: *New England J. Med.*, 238: 787, 1948.
3. COOKE, J. V.: *J. A. M. A.*, 119: 547, 1942.
4. MITCHELL, A. G. AND NELSON, W. E.: Textbook of Pædiatrics, W. B. Saunders Co., Philadelphia.
5. BRENNEMANN, J.: Practice of Pædiatrics, W. F. Prior Co., Inc., Hagerstown, Md.
6. DALE, J. H. JR.: *J. Pediat.*, 34: 421, 1949.
7. SNELLING, C. E., BROWN, A. AND ERB, I. H.: *Arch. Dis. Childhood*, 9: 315, 1934.
8. RIIS, J.: *Acta Pædiat.*, 33: 230, 1946.
9. WOLMAN, I. J. *et al.*: *Pennsylvania M. J.*, 52: 474, 1949.

ACTH AND CORTISONE IN THE TREATMENT OF ACUTE LEUKÆMIA*

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E. S. MILLS, M.D. and
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THE REPORTED OBSERVATIONS that increased adrenal cortical function in animals resulted in involution of normal lymphoid tissues,[1] that administration of compound E caused regression of a lymphoid tumour in mice,[2] and that alterations in adrenal cortical function occur in patients with lymphoid neoplasms[3] suggested that the administration of cortisone or the stimulation of adrenal cortical function with adrenocorticotropic hormone (ACTH) might influence favourably the course of acute leukæmia in man. Early reports indicated that these agents could induce remissions of the disease in both children and adults.[4 to 12] The follow-up observation periods were short and the final place of these hormones in the treatment of acute leukæmia remained to be determined.

Nine consecutive patients with acute leukæmia were treated with ACTH or cortisone at the Montreal General Hospital during the 12 month period December, 1949 to December, 1950. Despite this treatment all had died from the disease by June, 1951. Complete follow-up data are available for every case and autopsies were performed in 8 of them. A report of this small group seems justified because the discouraging results have not fulfilled the hope that this form of treatment would be of practical value in acute leukæmia.

CLINICAL MATERIAL AND METHODS

There were 5 male and 4 female patients in the group and their ages ranged from 10 to 60 years. Seven were suffering from acute granulocytic leukæmia, 1 from acute lymphocytic leukæmia and 1 from an acute undifferentiated "stem-cell" form of the disease. The presenting clinical picture varied but some or all of the following features were present in every case: malaise, weakness, weight loss, anorexia, fever, pallor, bone pain, a bleeding tendency and enlargement of lymph glands, liver and spleen. Peripheral blood studies showed a marked anæmia in all 9 patients, thrombocytopenia in 5 and a normal or low leukocyte count in 6. Bone marrow smears or sections showed the features of acute leukæmia in every case.

ACTH, cortisone or both hormones were given to each of the patients. Cases 1, 2 and 3 were treated solely with these agents. The others were given blood transfusions and penicillin as well. After trial periods on this regimen, cases 6, 7, 8 and 9 also received folic acid antagonists.

Cortisone was given as the acetate ("Cortone", Merck) by intramuscular injection in doses of 25 to 100 mgm. every 6 hours. ACTH ("Acthar", Armour) was given by the same route in doses of 10 to 25 mgm. every 6 hours. An initial daily dose of 400 mgm. of cortisone or 100 mgm. of ACTH was usually prescribed. A smaller amount was used for the 10 year old child. When side effects appeared the dose was reduced. If the side effects caused concern the hormone treatment was stopped. The total dose varied from

*From the Departments of Medicine and Pathology, The Montreal General Hospital and McGill University, and the Montreal General Hospital Tumour Registry.

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†Senior Medical Research Fellow, National Research Council, Canada.

TABLE I.

ANALYSIS OF RESULTS

Case number	Sex	Age	Type	Drug	Total dose mgm.	Other treatment	Hæmatologic remissions	Relapses	Remissions following relapses	Survival days	Side effects	Improvement in					
												Fever	Bone pain	Bleeding	Glands and spleen	Appetite	Outlook
1	F.	60	G	Cortisone	2,100	none	0	—	—	16	+	+	+	+	0	+	+
2	M.	45	G	Cortisone	2,675	none	0	—	—	11	+	0	—	0	0	0	+
3	F.	15	L	Cortisone	1,550	none	0	—	—	11	+	+	+	+	0	+	+
4	F.	17	G	Cortisone	6,125	blood	0	—	—	33	+	+	+	+	0	+	+
5	F.	48	G	Cortisone	4,475	blood aureomycin	0	—	—	120	+	+	+	+	0	+	+
6	M.	19	S	Cortisone	3,175	blood penicillin	0	—	—	26	+	+	—	+	+	+	+
				Cortisone	4,450	blood aminopterin penicillin	+	2	1	223	+	+	+	+	+	+	+
7	M.	17	G	Cortisone	1,300	blood penicillin	0	—	—	6	0	0	0	0	0	0	+
				Cortisone	4,200	penicillin aminopterin blood	+	1	—	13	+	+	+	+	+	+	+
				ACTH	425	blood penicillin	0	—	—	7	0	0	0	0	0	0	0
				ACTH	2,575	A-methopterin blood penicillin	+	2	1	143	+	+	+	+	+	+	+
8	M.	10	G	ACTH	200	penicillin blood	0	—	—	7	0	0	0	0	0	+	+
				ACTH	575	blood penicillin A-methopterin	0	—	—	15	+	0	0	0	0	+	+
9	M.	33	G	ACTH	2,300	blood penicillin	+	1	0	153	+	+	+	+	+	+	+
				ACTH	625	A-methopterin blood penicillin	0	—	—	19	+	+	0	0	0	+	0

case to case and the details are shown in Table I together with an analysis of the results.

RESULTS

Clinical.—During hormone therapy each of the 9 patients showed improvement in one, several or all of the following features: mental outlook, appetite, fever, bone pain, bleeding tendency, lymphadenopathy, hepatomegaly and splenomegaly. The improvement was manifest as early as 24 hours after starting treatment and was well established within a week. These changes were not necessarily accompanied by any hæmatologic improvement and they did not presage any striking prolongation of the survival time.

Hæmatologic.—Some data concerning individual cases are presented in Figs. 1, 2 and 3. A complete or partial return of the blood and bone marrow to normal was regarded as an

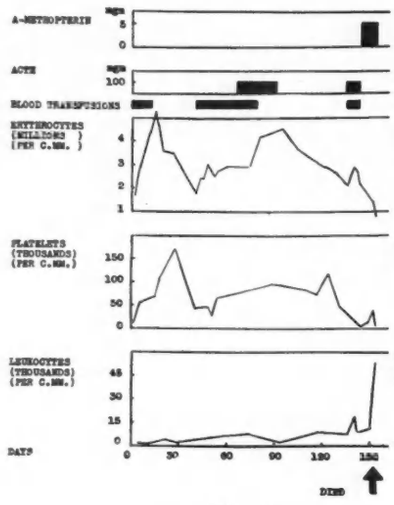

Fig. 1

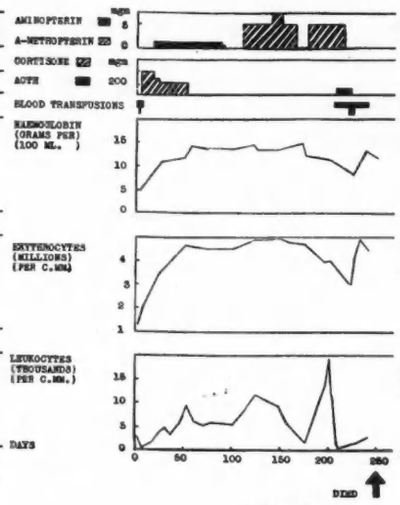

Fig. 2

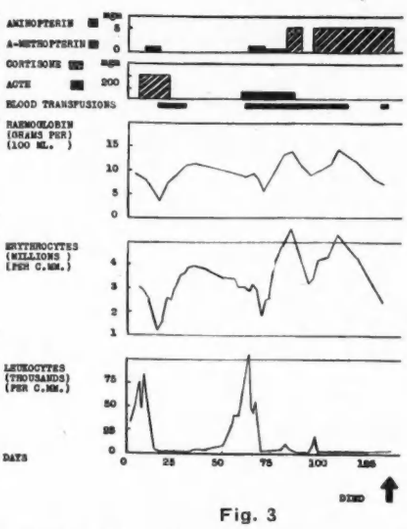

Fig. 3

Fig. 1. (Case 9).—Male, age 33, acute granulocytic leukæmia. **Fig. 2.** (Case 6).—Male, age 19, acute stem-cell leukæmia. **Fig. 3.** (Case 7).—Male, age 17, acute granulocytic leukæmia.

hæmatologic remission. A partial 2 week remission of this type occurred in case 9 during treatment with ACTH, blood transfusions and penicillin (Fig. 1). Hormone therapy alone or together with blood transfusions and antibiotic treatment did not induce hæmatologic improvement in the other 8 cases. However, a complete hæmatologic remission, which lasted 3 months, occurred in case 6 (Fig. 2) and a partial remission of 6 weeks' duration occurred in case 7 (Fig. 3) when a folic acid antagonist was given in addition to cortisone, blood transfusions and penicillin. This combined treatment did not result in any hæmatologic improvement in case 8 nor did it evoke a second remission in case 9.

Side effects.—The administration of ACTH or cortisone to patients can produce the clinical manifestations and metabolic alterations observed in spontaneously occurring Cushing's syndrome. Many of these side effects were observed in the present group of patients during hormone therapy. Œdema appeared in 6 cases. Acne, purplish abdominal striæ, moon-like facies and a buffalo hump appeared in 2 cases. Mental depression was a feature in 2 cases and glycosuria occurred in 1 case. None of the patients developed hypertension.

Duration of life.—Five of the patients died within a month, 3 others in less than 6 months and the longest survivor lived for only 9 months from the onset of the disease.

Autopsy findings.—Eight cases were examined post mortem with special reference to confirmation of the clinical diagnosis, to detection of any regression in the disease, and to alterations in the endocrine glands that might be related to hormone therapy. In each instance the clinical diagnosis of acute leukæmia was confirmed. The disease was of the stem-cell type in one case, lymphoblastic in one case and myeloblastic in the others. There was degeneration and necrosis of some leukæmic cells in one case but these changes were slight in relation to the large amount of well preserved leukæmic tissue. This patient (Case 7) had received aminopterin as well as ACTH. There was no histologic regression of the disease in the other cases. Leukæmic infiltration in one or more of the endocrine glands was demonstrated in some. There were no histologic changes in any of the endocrine glands which could be attributed to treatment. Adrenal cortical lipoid was depleted in several instances but this is often observed in other diseases. Hæmorrhagic lesions were seen in every case and in one of them a massive hæmorrhage into the lungs and intestinal tract was the immediate cause of death. Terminal bronchopneumonia was present in 3, staphylococcus septicæmia in one and acute non-specific enteritis in another.

DISCUSSION

The course of untreated acute leukæmia varies from case to case but the average duration of life is less than 2 months and most patients succumb within 6 months. "Subacute" cases may survive longer. Temporary spontaneous remissions have often been observed. In children as many as 10% experience a remission lasting several weeks but spontaneous remissions are rare in adults.

Blood transfusion was for many years the only effective palliative treatment. Maturation of myeloblasts was observed following blood transfusions[13] and a similar maturation effect has been seen following transfusions of fresh plasma, but not when reconstituted dried plasma or a gamma globulin fraction of plasma was used.[14] Most of the reported instances of remission in acute leukæmia have occurred in patients receiving transfusions of blood or plasma.[15] The use of complete exchange transfusions for treatment resulted in a high proportion of temporary remissions.[16] More recently it was shown that folic acid antagonists can induce temporary remissions in a significant but variable proportion of patients with the disease.[17] (See also paper by Laski *et al.* in this issue.)

Any evaluation of ACTH or cortisone in the treatment of acute leukæmia must take into account the history of the disease without treatment, and when other therapeutic agents are used. Conclusions concerning the value of these hormones, based on the results of small clinical trials, are apt to differ because of variations in the course of the disease from case to case, because treatment schedules are seldom identical, and because opinions vary as to what constitutes a remission.

Each of the patients in the present group showed some clinical improvement. No hæmatologic remissions occurred in the 3 cases who were given only ACTH or cortisone but hæmatologic remissions did occur in 3 of the others. It seems likely that folic acid antagonist therapy accounted for the improvement in 2 of these and it is possible that blood transfusions as well as ACTH played a part in inducing a remission in the other.

SUMMARY AND CONCLUSIONS

1. ACTH and cortisone were used in the treatment of 9 patients with acute leukæmia; 3 were treated solely with these hormones. The others were given blood transfusions and penicillin as well, and 4 of them also received folic acid antagonists.

2. Clinical improvement occurred in each of the 9 patients while hormone therapy was exhibited. This improvement was not necessarily accompanied by hæmatologic remission and did not presage any striking prolongation of survival time.

3. A partial hæmatologic remission occurred in one patient while receiving ACTH, blood transfusions and penicillin. Hormone therapy alone or together with blood transfusions and antibiotic treatment did not induce hæmatologic improvement in the other 8 cases. A complete hæmatologic remission occurred in one case and a partial remission of this type occurred in another when folic acid antagonist treatment was given in addition to cortisone, blood transfusions and penicillin.

4. Autopsies were performed in 8 of the cases. The clinical diagnosis was confirmed in each. There was no regression of leukæmic tissue or histologic alteration in endocrine glands which could be attributed to hormone therapy.

5. Five of the patients died within a month, 3 others in less than six months and the longest survivor lived for only 9 months from the onset of the disease.

6. It is concluded that ACTH and cortisone were of little practical value in the treatment of these 9 cases of acute leukæmia.

We are indebted to Mrs. H. L. Baker for her careful technical assistance.

REFERENCES

1. DOUGHERTY, T. F. AND WHITE, A.: *Proc. Soc. Exper. Biol. & Med.*, **53**: 132, 1943.
2. HEILMAN, F. R. AND KENDALL, E. C.: *Endocrinology*, **34**: 416, 1944.
3. DOBRINER, K., LIEBERMAN, S. AND RHOADS, C. P.: *Cancer Research*, **7**: 711, 1947.
4. FARBER, S., SCHWACHMAN, H., TOCH, R., DOWNING, V., KENNEDY, B. H. AND HYDE, J.: Proceedings of the First Clinical ACTH Conference, Blakiston, Philadelphia, p. 328, 1950.
5. DAMESHEK, W., SAUNDERS, R. H. JR. AND ZANNOS, L.: *Bull. New England Med. Centre*, **12**: 11, 1950.
6. SPIES, T. D., STONE, R. E., LOPEZ, G. G., MILANES, F., TOCA, R. L. AND REBOREDO, A.: *Lancet*, **2**: 241, 1950.
7. STICKNEY, J. M., HECK, F. J. AND WATKINS, C. H.: *Proc. Staff Meet., Mayo Clin.*, 25, **17**: 488, 1950.
8. PEARSON, O. H. AND ELIEL, L. P.: *J. A. M. A.*, **144**: 1349, 1950.
9. SCHULMAN, I.: *Am. J. Dis. Child.*, **80**: 521, 1950.
10. PEARSON, O. H. AND ELIEL, L. P.: *J. Clin. Investigation*, **29**: 838, 1950.
11. KINSELL, L. W., ROGERS, H., BAKER, C. AND JENKINS, B. J.: *J. A. M. A.*, **144**: 617, 1950.
12. BELL, R. E. AND THOMSON, R. K.: *Canad. M. A. J.*, **64**: 43, 1951.
13. SABIN, F. R., ASTURIAN, C. R., CUNNINGHAM, R. S. AND DOAN, C. A.: *J. Exper. Med.*, **40**: 845, 1924.
14. SCHWIND, J. L.: *Am. J. M. Sc.*, **213**: 170, 1943.
15. DREYFUS, B.: *Rev. d'hémat.*, **3**: 29, 1948.
16. BERNARD, J. AND BESSIS, M.: *Sang.*, **19**: 45, 1948.
17. FARBER, S., DIAMOND, L. K., MERCER, R. D., SYLVESTER, R. F. AND WOLFF, J. A.: *New England J. Med.*, **238**: 787, 1948.

In the treatment of Weil's disease the dosage of penicillin recommended is 250,000 units three hourly by the intramuscular injection route. If there are favourable responses after 24 hours it may be advisable to try doubling the dose. Penicillin should be continued for at least one week. A rise in temperature after the initial dose is a favourable sign.—Lawson, C. W., *Brit. M. J.*, **2**: 648, 1951.

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Dec. 1951, vol. 65

FOLIC ACID ANTAGONISTS IN THE TREATMENT OF LEUKÆMIA IN CHILDREN

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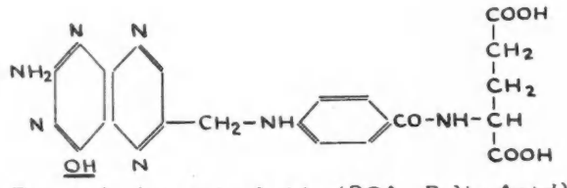
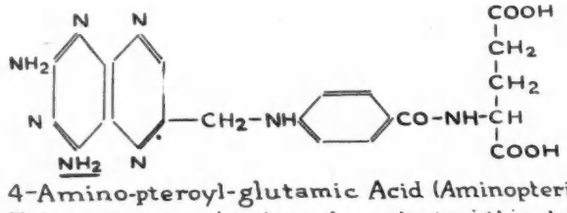
FOLIC ACID (pteroyl-glutamic acid) is a vitamin factor essential to practically all forms of life. This substance has been isolated in a chemically pure form and synthesized. A number of conjugates or analogues with chemical structures similar to folic acid have been synthesized. Some of these have the same properties as folic acid in regard to promoting the growth of certain test bacteria (*Lactobacillus casei* and *Streptococcus fecalis* R.). Others are biologically antagonistic to folic acid and inhibit its growth-promoting qualities. The most powerful of these folic acid antagonists is 4-amino-pteroyl-glutamic acid (aminopterin). Other conjugates of folic acid which are less antagonistic, are a-methopterin, amino-an-fol, an-fol-A, and met-fol-B. The formulæ and chemical structure of the various folic acid analogues are given by Farber.[1]

In Fig. 1, the structural formulæ of folic acid and aminopterin are shown. It may be seen at a glance how similar are the chemical configurations of these two compounds and yet biologically they are so diametrically opposite in their effect on living cells. Although the action of these antagonists is not completely understood it is assumed, because of their chemical similarity to folic acid that they are able to block an essential metabolic process in which folic acid is a necessary component.



Pteroyl-glutamic Acid (PGA, Folic Acid)



4-Amino-pteroyl-glutamic Acid (Aminopterin)
This substance is strongly antagonistic to Folic Acid

Fig. 1

Farber,[2] working with folic acid conjugates, biologically similar in their action to folic acid, in the treatment of various malignant diseases, detected in the tissues of children with acute leukæmia, what he termed "an acceleration phenomenon in the leukæmic process". From this he deduced that related compounds or analogues which were antagonistic to folic acid, might be efficacious in the treatment of leukæmia by retarding the process. Subsequent to his report of temporary remission induced in the acute leukæmias of children by folic acid antagonists, it was decided to assess this method of therapy in children with leukæmia or allied conditions admitted to the Hospital for Sick Children.

DIAGNOSIS

In all cases treatment was withheld until the diagnosis was assured. The diagnosis was made on the basis of history, clinical findings, peripheral blood studies, x-ray studies of bone, marrow aspiration and occasionally lymph gland biopsy.

It becomes apparent, when a series of cases of leukæmic children were studied intensively, that each case has more or less individual characteristics. Whether these are variations in the same disease process involving a common type of stem cell, or whether they represent fundamental differences, possibly involving separate cell types, it is difficult to determine. In our experience, in most cases of leukæmia in children it is impossible to determine with any degree of assurance the type of cell from which the leukæmic cell is derived. In most cases of leukæmia in children the blast cell is so anaplastic that a diagnosis of the cell type based on minor cytological differences is not valid. Occasionally, one may hazard an opinion as to the type of leukæmic cell by the company it keeps, either in the peripheral film or the bone marrow aspiration. It may be a confession of ignorance on the part of the writers, but in most cases of leukæmia in children, our diagnosis was simply acute leukæmia.

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METHODS OF TREATMENT

Fifty-three cases of leukæmia have been treated with folic acid antagonists. In 37, this was the only type of specific therapy attempted. In 16, the folic acid antagonists were used prior to or subsequent to treatment with ACTH or cortisone. The two antagonists used were aminopterin and a-methopterin. The former is approximately five times as toxic as the latter. As their effectiveness is proportional to their toxicity, there is little advantage in either chemical. The average dose of aminopterin was approximately 1 mgm. per day and that of a-methopterin 5 mgm. The dosage was continued until there was either an abatement of the leukæmia or signs of toxicity were evident. Both these effects usually appeared about the same time. In most patients a total of 7 to 10 mgm. of aminopterin or 35 to 50 mgm. of a-methopterin was given and then the treatment discontinued. These so-called "courses" were repeated as frequently as necessary until the tolerance of the patient was reached or it was obvious the leukæmic process was refractory to the chemicals. In some children an attempt was made to arrive at a maintenance dose but this was relatively unsuccessful in our hands. In two cases x-ray therapy was employed as well. In practically every patient, however, supportive treatment in the form of both direct and indirect transfusions and various antibiotics was liberally used. In the individual case, the use of supportive treatment, particularly blood transfusions might somewhat confuse the picture in regard to assessment of clinical or hæmatological improvement due to the drug therapy. However, as adjuvant treatment, particularly in children, is only of transitory benefit, any effect it may have had may be considered as inconsequential, and such effects have been taken into consideration in the evaluation of each case.

RESULTS

In appraising the effects of the folic acid antagonists in our series, it was found that according to their response, each patient might be placed in one of four main categories. This separation is of necessity arbitrary and there is in reality no sharp or definite division between the various types of response. The clinical and hæmatological criteria for each category are given below.

Category I.—This type of case temporarily responded dramatically to the administration of the folic acid antagonists. Following a latent period of four to seven days signs of general toxicity appeared. These consisted chiefly of increased irritability, lassitude and anorexia. Toward the end of this period a stomatitis might also develop which consisted of bleeding ulcers of various sizes on the gums, tongue, and buccal mucous membrane. After the first three to four days of treatment the total white blood count usually fell frequently to leukopenic levels with a relatively greater fall in the proportion of circulating blasts. At the same time the spleen, and lymph glands rapidly decreased in size. The administration of the chemical was usually stopped or the dose reduced because of the reduction of the white blood cells or signs of toxicity. By the end of the second week there was evidence of regeneration of the normal blood constituents. The reticulocyte count increased, immature but normal cells of the myeloid series began to appear in increasing numbers in the peripheral blood, and the platelet count which initially was usually at a low level approached normal.

The most important index of a remission was the state of the bone marrow, and in most of the cases 90% or more of the cells of the marrow at the time of the initial diagnosis were "blast forms" or primitive undifferentiated leukæmic cells. Concurrently with the improvement in the peripheral blood, the "blast forms" in the bone marrow were reduced to levels less than 4% and there was a flooding back of the normal marrow constituents. The marrow of these cases at the height of the remission could not be distinguished from a normal marrow. The child often resumed his normal activities and was to all appearances clinically normal. However, after a variable period of time usually from four to six weeks, there was a recurrence of the leukæmic picture in all its clinical and hæmatological aspects. After the first relapse, further treatment with the folic acid antagonists had much less effect. Attempts to arrive at a maintenance dose sufficient to keep the leukæmic process in abeyance was no more successful in our hands than an intermittent form of therapy. The number of patients in which such a clear-cut remission was produced, even though of short duration was a relatively small percentage of the total.

Category II.—These cases were similar to Category I, in that there was definite clinical

and hæmatological evidence of an abatement of the leukæmic process. But various manifestations of the disease still persisted. The enlarged lymph glands in some patients regressed in size but did not completely disappear. The enlarged spleen frequently became smaller but often remained palpable. Some blasts persisted in the peripheral circulation and although the blasts in the bone marrow decreased they were still present in excess of normal. Despite administration of the folic acid antagonists to the limit of the tolerance of the patient, a complete remission could not be obtained.

Category III.—These cases all showed the results of the toxicity of the drug and in addition the lack of an appreciable differential effect of the therapy on the leukæmic and the normal cells. At no time in these patients was there any evidence of clinical improvement that could not be explained on the basis of supportive therapy. After varying period of time and dosage, a rapid fall in the white blood count occurred with concomitant decrease in the size of spleen and peripheral lymph glands. The platelets, usually low at the onset, fell to still lower levels. Although the "blast forms" usually disappeared from the peripheral circulation, there was no evidence of regeneration of the normal blood constituents, and these patients, in spite of repeated transfusions and antibiotic therapy, died of multiple hæmorrhages from various sites and frequently generalized sepsis. Invariably at post-mortem, these children showed minimal evidence of the usual leukæmic infiltration except for possibly a few residuals in some of the lymph glands and the bone marrow. The latter was usually hypoplastic. There is little doubt that folic acid antagonists caused a marked regression on the leukæmic cells, but apparently the normal blood-forming tissue was at the same time so depressed that it was unable to regenerate.

Category IV.—In this type of case there was at no time any clinical hæmatological evidence that the therapy had any significant effect. Most of these patients received prolonged and intensive therapy, and the normal tissue as well as the leukæmia cells seemed to be more resistent to the toxic effects of the drug. All of these cases which came to post mortem showed the classical widespread infiltration with leukæmic cells which was so strikingly absent in many of our other treated cases. Apparently this type of reaction to the folic acid antagonists is more common in adults with leukæmia.

TABLE I.

LEUKÆMIA IN CHILDREN
FOLIC ACID ANTAGONISTS ONLY USED

Type of response	*Number of patients*
Category I	4
Category II	5
Category III	17
Category IV	11
Total	37

In Table I are shown the results of 37 children in which the folic acid antagonists were the only specific therapy. In approximately 25% there was a partial or complete remission of varying duration. Fig. 2, is a graphic representation of the

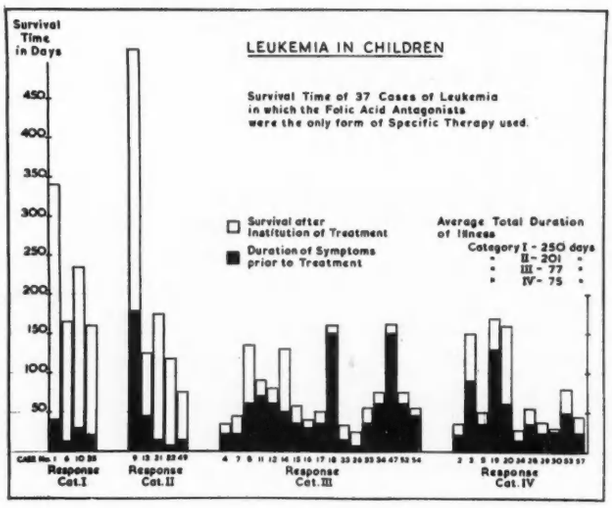

Fig. 2

disease process of this group of children with an approximation of the total length of their illness and the duration of life after the beginning of therapy.

The average expected survival of acute leukæmia in children not receiving specific therapy is less than 90 days.[3] It is considered that in category I and II, there was significant prolongation of life, as the average survival time of those with either a complete or partial remission was in excess of 200 days. Certainly in these 9 patients there was no case of chronic leukæmia and it is extremely unlikely that 25% of a series of leukæmia in children would be of the subacute type. Although our series of cases is too small for statistical analysis, it is our impression that the aleukæmic or subleukæmic type of leukæmia with a low or normal white blood count is relatively a more benign type of disease and responds better to specific therapy.

There is little doubt that treatment hastened the death in some of the patients falling into category III. Even though the total dosage was small, many of these patients, shortly after therapy was started, quickly passed into a profound hypoplastic phase in regard to both leukæmic cells and normal marrow constituents. The child usually succumbed in a few days from hæmorrhage and/or sepsis in spite of vigorous supportive therapy.

There is apparently a marked individual variation in susceptibility to the action of the folic acid antagonists. This effect apparently bears little relationship, except within wide limits to the age of the child, the duration, and the type of leukæmia. This is well demonstrated in the contrast between categories III and IV. In the latter the chemicals were frequently given in relatively large doses for long periods of time with only minor evidence of toxicity and no clinical or laboratory evidence of any effect on the leukæmic process, whereas in category III, relatively small amounts of the chemicals produced striking changes.

There was an additional group of 16 patients in which the folic acid antagonists were used either prior to or subsequent to treatment with ACTH or cortisone. In every case the sands had run out as far as the usefulness of the initial method of treatment was concerned. The switch to the other type of therapy, in addition to being obvious, was the only alternative. There was very little correlation between the response to the two types of treatment. Some cases responded well to the hormone and poorly to the chemicals and the converse was also true to some extent. An occasional patient was resistant to both forms of treatment. However, even in this small series of cases it is apparent from the results that a patient may become refractory to the continued use of either the folic acid antagonists or ACTH and cortisone and yet have a remission of considerable degree when the patient is changed to the alternative method of treatment. Thus, in some patients at least, the combined employment of the hormones and the folic acid antagonists may offer slightly more than will either form of therapy alone.

Table II is a summary of all the cases of leukæmia in which the folic acid antagonists were used. The category of response was judged entirely by the reaction of the patient to the antagonists and not to the effects of any previous or subsequent treatment with ACTH or cortisone.

TABLE II.

LEUKÆMIA IN CHILDREN
ALL CASES IN WHICH THE
FOLIC ACID ANTAGONISTS WERE USED

Type of response	*Number of patients*
Category I	4
Category II	9
Category III	23
Category IV	17
Total	53

DISCUSSION

From experimental work it appears that folic acid is necessary for the growth and multiplication of cells. Hence one would expect that the folic acid antagonists would be able to produce a relatively greater deficiency of folic acid in those cells which are undergoing rapid growth and multiplication. This probably accounts for their action on leukæmic cells and this effect is likely more of a relative than a specific or selective effect. The failure of the folic acid antagonists to have any appreciable effect on the chronic leukæmias of adults and a significant proportion of leukæmias in children could be explained on the basis that in these cases the differential between the effects of the folic acid antagonists on normal cells and leukæmic cells was not sufficient to produce any appreciable effect on the leukæmic process before the overall toxicity of the folic acid antagonists manifested itself. One argument against the assumption that the folic acid antagonists produce a folic acid deficiency is that in none of our cases was there any evidence of the development of a macrocytic or megaloblastic type of reaction in the erythroid elements which is regarded as one of the features of folic acid deficiency.

Whatever is the mode of action of these drugs, there is no doubt that in some of the acute leukæmias of children a dramatic temporary, clinical and hæmatological remission can be produced. These remissions were not sustained for any appreciable period of time and subsequent relapses were less amenable to treatment. In some cases, judging by the findings in the peripheral blood and the bone marrow, one appears to be able to keep the leukæmia under control with continued therapy, but the normal hæmopoietic tissue seems to lose its ability to regenerate and the

patient finally succumbs because of an insufficient supply of normal leukocytes and platelets.

Obviously these chemicals can in no way be considered as a cure for leukæmia, and from a practical point of view, they cannot even be considered as a very satisfactory form of therapy. However, in a few cases their use has definitely produced a remission and prolonged the life of the patient. During these remissions the patient had a relatively normal and comfortable existence for a limited period of time.

The ultimate failure of this type of treatment should not be cause for depreciation nor despair, but rather it should be considered as an important step in our understanding of this disease. It is an indication that the control of a malignant cell may be possible by interference with its metabolism. As information accumulates concerning the metabolism of normal and malignant cells, perhaps fundamental differences, either qualitative or quantitative will be uncovered. In such an event it is quite possible that suitable inhibitors to malignant cells may be found. As this has been achieved to a remarkably successful degree with regard to infectious agents, it is hoped that ultimately the same success may be attained with regard to neoplastic diseases.

CONCLUSIONS

1. The folic acid antagonists aminopterin and a-methopterin were used in the treatment of 53 cases of leukæmia in children.

2. In no case was a permanent cure obtained, but in 13 patients or 26%, there was a complete or partial clinical and hæmatological remission of short duration with some prolongation of life.

3. Except for transient episodes of toxicity, in general those patients which responded favourably were maintained in reasonably good health until shortly before death.

4. The development of a refractory state to the administration of the folic acid antagonists did not preclude the possibility of a remission with an alternative type of treatment.

REFERENCES

1. FARBER, S.: *Blood* (J. Hematol.), 4: 160, 1949.
2. FARBER, S. *et al.*: *New England J. Med.*, 238: 787, 1948.
3. RODGERS, C. L., DONOHUE, W. L. AND SNELLING, C. E.: Leukæmia in Children. (This Journal).

ACTH AND CORTISONE IN THE TREATMENT OF LEUKÆMIA IN CHILDREN

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IT IS NOT WITHIN THE SCOPE of this communication to review or recapitulate the various physiological and biochemical phenomena associated with the exhibition of the hormones ACTH and cortisone. By now it is well known that the administration of either ACTH or cortisone can bring about profound alterations in the total metabolism and cellular reactions of an individual in such a manner that the usual course of many diseases is dramatically modified or even temporarily reversed.

Our interest in the possible use of these drugs in the treatment of leukæmia was first aroused in 1949. As there was an accumulation of experimental data in both man and animals that activity of the adrenal cortex had a depressing effect on lymphoid tissue, lymphocytes, and eosinophils, there was some indication that this was a rational method of approach. The temporary but apparently complete remission induced in a patient with eosinophilic leukæmia by ACTH at the Hospital for Sick Children[1] and word-of-mouth reports concerning favourable responses with similar forms of treatment in other centres stimulated us to further investigate the possibilities of this type of therapy.

METHODS

The diagnosis of leukæmia was made on the basis of history, physical examination peripheral blood, bone marrow aspiration and occasional biopsy. Prior to and during treatment daily blood examinations including absolute eosinophile counts were done. Repeated marrow aspirations were performed at approximately weekly intervals depending upon the apparent clinical and hæmatological progress of the patient. All the patients in addition to the hormone therapy received as adjuvants

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blood transfusions, antibiotics and symptomatic treatment as indicated. Although considerable chemical data were collected in regard to blood and urine, because of the limitation of facilities it was not possible to do complete chemical and/or balance studies on all patients particularly the younger children who were incontinent of urine and fæces.

As the study progressed, variation in the type of treatment was of necessity dependent upon several factors, such as limitation in the supply of hormones, age of the patient, response to treatment and potency of the lot of hormone. Dosage varied widely, with ACTH from 10 to 200 mgm. per day and with cortisone from 50 to 200 mgm. per day. Usually fairly large doses were given initially and subsequent doses reduced to a level that was just sufficient to keep the peripheral blood free of eosinophil or at a level of 1 to 5 per c.mm. This criterion was obviously of little use when initially the peripheral blood contained few eosinophils. Several of the patients had been previously treated with one or more of the folic antagonists (aminopterin and a-methopterin). The patients were maintained on a low sodium diet. Therapy was continued until a remission was obtained or there was no evidence of continued improvement. If the usual signs and symptoms of the disease had regressed, the peripheral blood had returned to normal and the blast forms in the marrow had been reduced to less than 4% it was considered that a complete remission had been effected. Side effects such as excessive sodium retention, hypertension and occasionally convulsions were accepted as indications that the dosage of the hormone should be reduced. In our experience there were wide variations in the potency of different lots of ACTH and the dosage had to be adjusted according to the effects any particular lot of ACTH produced. With potent lots of ACTH, 25 to 50 mgm. per day in 6 divided doses were administered intramuscularly. Lately ACTH has been given by continuous intravenous. By this method the same effect is achieved with approximately half the quantity used intramuscularly, *i.e.*, 10 to 20 mgm. per 24 hours. Our experience with cortisone has been somewhat limited because in our hands it was felt that the therapeutic response was more sluggish and the dramatic clinical improvement was usually lacking. However, in other centres cortisone, particularly the oral form, is the treatment of choice in the therapy of leukæmia. Cortisone has also a decided advantage in that it is not absolutely necessary to hospitalize the patient. When relapse occurred retreatment was instituted using either the original hormone or the alternative. When a patient obviously became refractory to further hormone therapy, he was treated with one of the folic acid antagonists and in some cases the hormones and the folic acid antagonists were used alternatively.

RESULTS

In all, 37 children suffering from leukæmia were treated with ACTH and/or cortisone. In this series there were 20 males and 17 females varying in age from 15 months to 14 years. All cases were judged to be of the acute variety, as the antecedent history of each patient and the clinical condition at the time of first admission indicated that the expected survival time without treatment would have been less than one year. Periods of treatment which resulted in a complete remission varied from 15 to 35 days. No clinical evidence of potassium deficiency was encountered and in general there was little difficulty with side effects although as the treatment progressed, the "Cushing-like" facies usually became quite evident. In a few cases the hormone therapy had a partial and very temporary beneficial effect both clinically and hæmatologically. In these patients the response was usually only apparent during the administration of the drugs and they quickly relapsed to their former state following cessation of the treatment. Table I shows the over-all results of the hormone therapy.

TABLE I.

TOTAL 37 CHILDREN WITH LEUKÆMIA TREATED WITH ACTH OR CORTISONE

One or more temporary but complete remissions	19
Incomplete or partial remission	4
No demonstrable effect on the leukæmia process	13
Apparent aggravation of the disease	1

The types of leukæmia and the results of treatment in the various categories are as follows:

(a) In one case of eosinophilic leukæmia two remissions were obtained.

(b) There were 3 patients which were diagnosed as acute granulocytic leukæmia. In Case 60 the hormone therapy had no appreciable effect. In Case 67 the treatment resulted in an apparent aggravation of the leukæmic process. This was the only reaction of this nature that was encountered in our series. A typical remission was obtained in Case 68. This last patient prior to any specific therapy had had a "spontaneous" remission following measles.

(c) The remaining 33 patients were classified as acute leukæmia. In this group complete remissions were obtained in 17 cases, partial remissions or clinical abatement in 4, and no effect in 12.

The duration of the temporary remissions induced, varied considerably, from 14 days to 243 days. Although the number of cases is too small to arrive at a definite conclusion it is our impression that longer remissions were obtained in those patients with low peripheral white blood counts. Following relapse, the response to retreatment was usually either more sluggish than initially, or there was no appreciable effect. Of fifteen patients which were treated after this first relapse only six responded with a second remission and in all of these the second remission was of shorter duration than the first. Three children were retreated for the third time and in one of these a third remission was obtained.

ACTH was used initially in the treatment of 31 leukæmic children and complete remissions

were obtained in 17. There was a partial or incomplete response in 4 patients, no response in 9, and an apparent acceleration of the disease process in 1. In 6 patients cortisone was given initially and in this group there were two remissions and in 4 there was no response.

From a study of 152 cases of leukæmia admitted to the Hospital for Sick Children who received no specific form of therapy it was determined that the average duration of life from the onset of symptoms was 130 days.[2] In this series of 37 patients, in the 18 patients which did not respond with a complete remission, the average duration of life was 118 days, which is comparable to cases receiving no specific form of therapy. However, as the average duration of life in the 19 which did respond with a remission was 247 days, it seems reasonable to assume that in this latter group there was definite prolongation of life.

Charts 1 and 2 illustrate the detailed hæmatological observations in a boy treated with ACTH in which a remission was produced.

According to our observations, in a patient who responds well to ACTH or cortisone therapy, the following is the usual sequence of events in regard to the hæmatological findings: decrease or disappearance of the circulating eosinophils, reduction or disappearance in the numbers of blast forms in both the peripheral blood and the marrow, regeneration of the erythroid elements and finally reappearance of granulocytic cells and platelets. The latter may occasionally make an explosive appearance, increasing from 20,000 to over 200,000 within 24 hours.

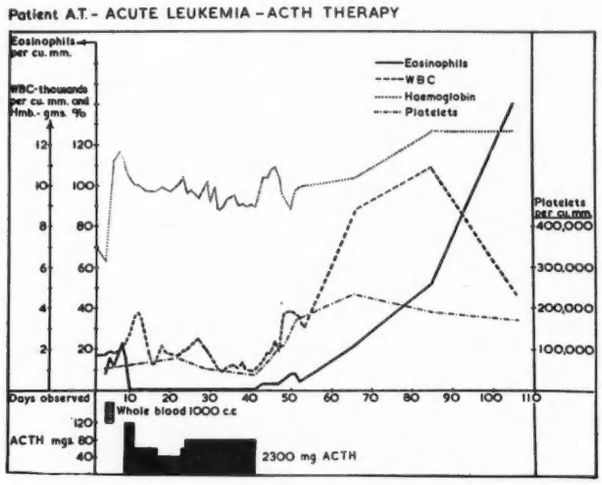

Chart 1

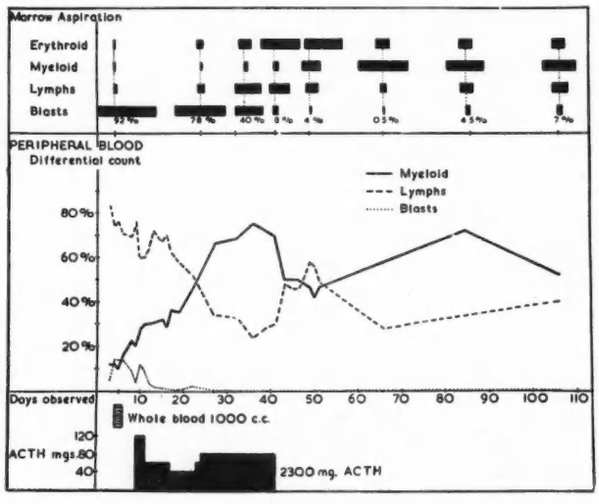

Chart 2

CHEMISTRY

In those patients in which chemical studies were undertaken, determinations were made of the urinary excretion of sodium, creatinine, creatine, uric acid, total nitrogen and neutral 17 ketosteroids. For a base period of 3-4 days and during the course of treatment the patients were maintained on a standard low sodium diet (approximately 2 gm. Na per day). No attempt was made to do exact balance studies.

Data were collected during 14 courses of treatment with ACTH on 9 patients. Fortuitously, during seven of these treatments a satisfactory remission was produced and in seven the hæmatological response to the hormone was minimal or ineffective.

Although there were no marked differences between the cases which responded and those which did not, in general the following trends were noted in regard to the chemical effects. There was normal sodium excretion when the hormone appeared to have the most beneficial clinical and hæmatological effect. Decreased sodium excretion frequently occurred when the patients were refractory to treatment. There was no significant difference in the excretion of creatine, uric acid, and total nitrogen in those patients which responded favourably and in those which did not. However, in a few cases the rate of uric acid excretion appeared to be proportional to the rate of disappearance of the blast forms from the peripheral blood and bone marrow. There was a definitely greater rise in the neutral 17 ketosteroids excretion in that group in which a satisfactory remission was pro-

duced. In those patients in which a complete remission did not occur, the 17 ketosteroid excretion was greater during the period when the treatment appeared to have the best clinical and hæmatological effect and later decreased even though the same or larger doses of ACTH were employed. Variations in the 17 ketosteroid excretion were probably directly related to the potency of the ACTH.

COMMENT

Experience at The Hospital for Sick Children and reports from other centres have established the fact that temporary remissions can be induced in the leukæmia of children by the administration of ACTH or cortisone.[3] In approximately 50% of our series an apparently complete remission was produced and in many of these children the improvement was so dramatic that at the fastigium of the remission there was no clinical or laboratory evidence of leukæmia.

To explain the action of ACTH and cortisone, it may be postulated that as a part of the effect of the increased physiological activity of the adrenal cortical steroids, induced or supplied by the hormone therapy, a milieu is produced which is so unfavourable to the leukæmic cells that the majority of them are destroyed and the effect is thus analogous to various carcinolytic agents which have been employed in the past. There is considerable evidence to support this concept. There is no flooding into the peripheral circulation of maturing or adult white cells proportional to the disappearance of the leukæmic cells from the peripheral circulation, and the decrease in the size of the lymph nodes and spleen. Repeated marrow aspirations prior to and during the administration of the hormones indicate that there is a marked decrease in the total nucleated cell population of the marrow coincident with a decrease in the proportion of blasts, and subsequently there is a reappearance of normal marrow constituents and a rise in the total nucleated count to normal. Chemical studies by Pearson *et al.*[4, 5] and our own findings that the relative increase in excretion of uric acid and creatine appear to be proportional to the disappearance of the leukæmic cells, indicate a considerable breakdown of tissue particularly in the early stages of hormone therapy. If leukæmia is fundamentally a neoplastic process it may be that after a shorter or longer period of time the leukæmic cells become adapted to the altered environment and thus refractory to further treatment.

A more optimistic concept, which to date has little evidence to support it, is that the leukæmias are not neoplastic processes but rather they represent a deficiency or block at some stage in the development or maturation of the white blood cells. In an attempt to compensate for the deficiency of normal white cells there is an outpouring of abnormal immature forms.

Although the administration of ACTH or cortisone in the acute leukæmias of children results in side effects which are evidence of either a distortion or over-activity of their normal physiological function, in their action on the hæmopoietic and lymphoid tissue, temporarily at least, they appear to supply or mediate the production of a substance necessary for normal activity. A hypothetical maturation factor may be mobilized in sufficient quantities to initiate normal development of the white cells by the mass action of these steroids. Coincident with this there is an elimination and destruction of the unusable and imperfect immature cells. Complete depletion of such a maturation factor may explain both the temporary effect of the hormones and their failure to be effective in some leukæmias.

From a therapeutic aspect, the disappointing feature of ACTH or cortisone therapy is the evanescent nature of the remission and the sluggish or refractory response to further treatment. There is, however, little doubt that in the leukæmias of children with the administration of ACTH and cortisone, more complete hæmatological and clinical remissions can be obtained in a higher percentage of cases and with less toxic effects than with any other therapeutic agents thus far employed. A valuable tool has been added to the armamentarium of the investigator.

SUMMARY

1. The results obtained in the treatment of 37 cases of leukæmia in children with ACTH and/or cortisone are presented.

2. Complete but temporary remissions occurred in approximately 50% of the patients.

3. None of the patients could be considered as cured or permanently benefited. Although repeated remissions were obtained in a few children, all eventually became refractory to further hormone therapy.

4. ACTH and cortisone although unsatisfactory for the permanent treatment of leukæmia in children are valuable tools in the further investigation of this disease.

REFERENCES

1. DONOHUE, W. L., SNELLING, C. E., JACKSON, S. H., KEITH, J. D., CHUTE, A. L., LASKI, B. AND SILVERTHORNE, N.: *J. A. M. A.*, **143**: 154, 1950.
2. RODGERS, C. L., DONOHUE, W. L. AND SNELLING, C. E.: Leukæmia in Children. A Review of 158 Cases. In this Journal.
3. Proceedings of the Second Clinical ACTH Conference 1951. Vol. II, pp. 251-288. The Blakiston Co., New York, Philadelphia, Toronto. Edited by Dr. John R. Mote.
4. PEARSON, O. H., ELIEL, L. P., RULON, W. R., DOBRINER, K. AND RHOADS, C. P.: *Cancer*, **2**: 943, 1949.
5. PEARSON, O. H., ELIEL, L. P. AND TALBOT, T. R. JR.: *Bull. New York Acad. Med.*, **26**: 235, 1950.

ACTH AND CORTISONE IN THE TREATMENT OF PEMPHIGUS ERYTHEMATOSUS

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PEMPHIGUS, in its many clinical forms, apart from the ocular variety, is a serious and usually a rapidly fatal disease. The cause is unknown and the treatment to date has been mainly supportive, depending on good nursing care and the trial use of drugs which are legion, and which have ranged from arsenic and vitamins to the antibiotics. However, whereas remissions are known to occur, spontaneously or otherwise, especially in the erythematosus variety, the course is nevertheless downhill, and death generally ensues from months to several years after the onset of the disease.

The case herein reported is deemed interesting because of the striking favourable results obtained with repeated courses of ACTH and the apparent lack of response to cortisone on two occasions with the dosage used. The ACTH was administered intravenously as an aqueous solution and intramuscularly, both as an aqueous solution and in a slow absorbing oily medium.

CASE REPORT

Mrs. J.D., aged 47, a white female, was first seen on March 24, 1948, with a history of having developed a pruritic scaly crusted eruption on the trunk the previous summer. The present episode had begun two months previously with maculo-crusted and denuded lesions on the chest and back, in the mid line areas and on the scalp. There also were two red macular lesions on the hard palate. The patient complained of very severe burning and irritation of the affected areas, which has remained a prominent feature of the disease. Differential diagnosis entertained at that time was: (1) seborrhœic dermatitis; (2) dermatitis herpetiformis; (3) Senear Usher disease (pemphigus erythematosus). Patch tests to 30% potassium iodide and 30% potassium bromide in petrolatum were positive. A skin biopsy of an early lesion was suggestive of dermatitis herpetiformis. The patient was intolerant to sulfapyridine and showed no response to liquor potassium arsenitis.

In May 1949, bullæ appeared on the forearms and the trunk and an erythematous crusted eruption involved the entire face. These persisted despite hospitalization with careful nursing, along with vitamin C and nicotinic acid, penicillin, streptomycin and aureomycin therapy. The laboratory findings, while in the Vancouver General Hospital, June 1949, were: red blood cells 4,270,000, hæmoglobin 80%, white blood cells 8,700, differential count—lymphocytes 23, monocytes 4, polymorphonuclears 70, eosinophils 2. Sedimentation rate was 66 mm. in one hour; total serum protein 6.5, albumin-globulin ratio 3.9/2.6; urine—negative.

The Nikolsky sign was now positive and a biopsy taken in July, 1949, of a bulla on the left arm revealed the histological picture compatible with the diagnosis of pemphigus erythematosus. This diagnosis was concurred in by members of the Pacific Northwest Dermatological Association, who saw this patient on October 20. Other therapeutic measures which were tried without success at this time were transfusions, antihistaminics, acetarsone, œstrogens in the form of premarin and diethylstilbesterol and progesterone. The use of stilbesterol appeared to be accompanied by an increase in the severity of the disease. Vitamin B_{12} was attempted as was desoxycorticosterone with vitamin C. These measures failed to arrest the rapid deterioration of the patient. Clinical improvement did seem to follow the use of testosterone proprionate, given intramuscularly, starting with 25 mgm. daily for three injections and increasing to 100 mgm. three times weekly. This hormone was discontinued however, because of the acute depression accompanying its use.

In December 1949, the patient, who was then desperately ill, developed recurrent gall bladder dyspepsia so severe that she refused nourishment. This necessitated surgical intervention, both to relieve her pain and in the hope that the infection in the gall bladder had been a contributory etiological factor in the production of the skin condition (Fig. 1).

On March 11, 1950, a successful cholecystectomy was performed. The postoperative course was completely uneventful. Healing occurred rapidly by primary intention in spite of the severe generalized skin involvement. The patient was discharged home on April 1, where she continued her rapid downhill course. She became melancholic and exhausted as a result of the burning and pruritus of her entire body surface. Her weight had gone down from 148 lb. in March 1949, to 100 lb. at the time of her admission to St. Paul's Hospital in July, 1950, for a trial of cortisone and ACTH.

On admission, the patient presented the clinical picture of a generalized exfoliative dermatitis with bullous lesions. The face was puffy and was covered with an erythematous crusted eruption. Both legs were entirely denuded with resulting contractures at the knee joints. Subjectively, there was intense burning and generalized pruritus with resulting insomnia which could not be relieved with sedation. She was extremely sensitive to temperature changes and trembled on the slightest exposure. Her mental state was one of fatigue and depression.

Cortisone was begun on July 20, using 300 mgm. in the first 24 hours, followed by 200 and then 100 mgm. daily. The circulating eosinophil count which was 1,700 at the onset of treatment, fell to 80 in 72 hours, and the skin showed definite improvement, during the first week of treatment. The face and neck did not share in this improvement, but the remainder of the body surface became dry. No new bullæ appeared and large areas of apparently normal skin became visible between the crusted lesions. However, the subjective symptoms did not become any less severe and by the ninth day

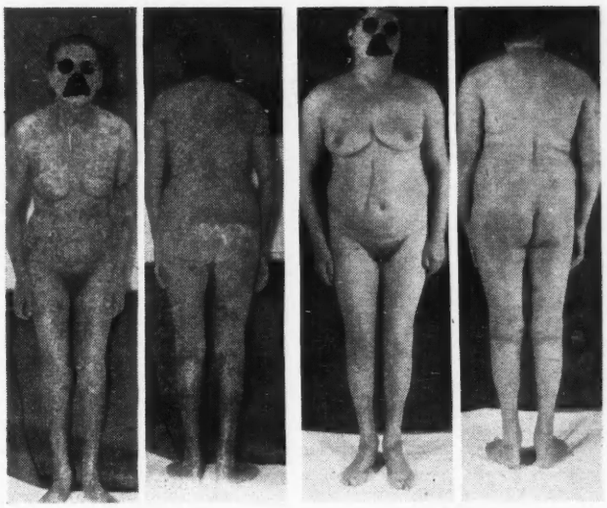

Fig. 1 Fig. 2

Fig. 1.—Clinical picture, January 23, 1950, prior to cholecystectomy and ACTH therapy. Fig. 2.—Clinical picture on June 7, 1951, after 11 months of ACTH therapy.

of cortisone therapy, the eosinophil count had risen to 1,000, remained at this high level and the skin condition had relapsed. The cortisone dosage was therefore increased to 200 mgm. daily, the eosinophil count dropped to 500 and the skin again improved slightly for a short period. On August 9, 1950, when cortisone was discontinued after treatment with 3 grams over a period of 20 days, the patient was no better than she had been at the onset, and no undesirable side effects had been encountered.

In view of the high eosinophil count, and of the improvement which appeared to accompany the fall in this count, ACTH was tried to see whether the reduction in the eosinophils would be paralleled by improvement in the clinical condition. ACTH 25 mgm. every 6 hours, was begun August 25, and was continued until September 23, the dosage being adjusted from time to time according to the needs of the patient and the availability of the drug.

It was noted that the patient began to gain weight immediately, increasing from 104 to 120 lb. in three weeks. At no time was there any observable œdema. Subjectively, the intense burning and itching began to subside after 24 hours, and by the fifth day, there were practically no complaints, not even when hyperæmia and the occasional moist lesion could be demonstrated on the skin. The circulating eosinophils remained consistently below 100. During this period, the only skin abnormality was a redness and scaling of the face and neck. For the first time in two years, the patient was willing and able to have a tub bath.

On September 21, the patient was given 50 mgm. of ACTH to determine how long a single injection would remain effective. After eight and a half hours, she began to complain of burning and irritation and after eleven hours the discomfort was so intense that regular treatment was resumed. Upon withdrawal of therapy, bullæ appeared on the forearms within twenty-four hours and by the end of the week, the patient was dejected, the skin shed in large sheets, leaving a burning pruritic raw surface. The hæmatocrit reading rose to over 50 when the skin condition deteriorated.

Hence it was noted that treatment with ACTH 80 to 140 mgm. daily, resulted in a remission with improvement in general health, gain in weight, fall in sedimentation rate, clearing of skin lesions, and absence of itching and burning sensations. Lesions returned within twenty-four hours after withdrawal of therapy and the exacerbation was severe in one week.

A second course of cortisone (2 gm.) was begun on September 30, after the patient had been without treatment for seven days; 300 mgm. were used in the first 24 hours at which time she developed marked precordial distress, and threatened circulatory collapse. Cortisone was discontinued for 24 hours after which it was given in 100 mgm. daily dosage. After a very slight transitory improvement, the skin again flared up and the patient became very depressed.

ACTH 25 mgm. was given once daily along with the cortisone with no benefit, nor was there any bnefit from the daily intravenous injection of ascorbic acid 1,000 mgm. along with the cortisone. On one occasion, 50 mgm. of cortisone dissolved in a bland ointment base was applied directly to the head and neck. This produced a local flare in the skin lesions which may have been attributable to the ointment base rather than to the cortisone.

By October 13, the skin had deteriorated, the patient had lost weight, the eosinophil had remained elevated, and the sedimentation rate had varied from 80 to 120 mm. for one hour. The patient was irritable and dejected and refused further cortisone.

A further course of ACTH (2 gm.) was then begun using up to 150 mgm. daily at 8 hour intervals. Subjective improvement was immediate. Weight gain again occurred from 120 to 132 lb. The sedimentation rate fell to 30 mm. in one hour. The skin lesions however, did not show the dramatic improvement seen with the first course of ACTH. Nor was there as significant or sustained a drop in the circulating eosinophils. It was noted that when a new batch of ACTH was begun, the eosinophils showed a marked fall and the skin a decided improvement. Testosterone aqueous suspension 25 mgm. 3 times daily was tried in an attempt to maintain the improvement obtained with the ACTH. The patient became acutely ill with emesis and chills. She became depressed and almost suicidal and the skin flared up with complete exacerbation in 24 hours. This again responded to aqueous ACTH intramuscularly. The high cost of the drug made it necessary to discontinue treatment at this time.

At home, the general condition deteriorated rapidly necessitating re-admission to hospital in January, 1951. During this admission, she was brought under control with ACTH 25 mgm. daily given as a continuous intravenous drip in 1,000 c.c. of 5% glucose in water. This method of administration proved to be most efficacious and above all, economical.

At this time, adactar-0-40, a new preparation of ACTH in oil for intramuscular use was made available. She was given 50 mgm. twice daily and was discharged from hospital on this dosage, clinically well. On April 16, the patient of her own accord reduced the dosage to 60 mgm. once daily.

She has been followed at weekly intervals. On this regimen her general condition remains splendid. She has developed an almost pathological appetite which she finds it impossible to control, and has shown a continuous weight gain with the appearance of moon face (Fig. 2). Occasional small bullæ occur which are not irritating and heal rapidly. Firm erythematous areas develop at the site of injections which are tender and pruritic, but gradually involute.

The sedimentation rate has been moderately elevated. The white blood count has varied between 12,000 and 17,000 per cubic millimetre. The circulating eosinophils have averaged about 200, the non-protein nitrogen has remained between 40 and 45 mgm. % and the blood cholesterol under 200 mgm. %. The blood sugar became elevated for some weeks but has subsequently returned to normal with moderate dietary restriction.

DISCUSSION

A patient with pemphigus was studied for 3 years under ideal conditions. She had the benefit of good nursing, of carefully controlled diet, of indicated laboratory investigations and of a

great variety of therapeutic agents. The following sterols were given a trial—œstrogen, progestrone, testosterone, desoxycorticosterone and cortisone. Finally, ACTH was used in aqueous solution both by the intramuscular route, and as a continuous intravenous drip, and at present, a slow-acting oily suspension is being given by intramuscular injection.

Whereas all other drugs in the dosage used were without effect in controlling this condition, ACTH caused immediate and dramatic improvement, both in the general well-being of the patient, in her mental state and in her skin lesions. This improvement has been sustained as long as the drug is administered.

Three methods of ACTH administration have been employed. It is apparent in this case that the use of aqueous ACTH by the intramuscular route is the most costly, requiring about 125 mgm. daily for maintenance. It has the added disadvantage of requiring at least three injections a day. The intravenous drip method is the most rapidly effective as well as the most economical. It is possible that as little as 5 mgm.[1] a day may be adequate. However, this is a hospital procedure, trying to the patient and at best is only practical for short term treatment.

The ACTH in oil offers great promise for an adequate economical ambulatory form of therapy, obviating the need for multiple injections and for hospitalization, and reducing the total daily requirement of the hormone.

A psychological study of this patient was most instructive. The patient, an intelligent co-operative, well-adjusted middle-aged female, had suffered a long debilitating and painful illness. At the time of her second hospital admission, she was emaciated, exhausted, crippled and almost moribund. With ACTH therapy, she became once more a healthy woman with a mild skin condition. At all times, she suffered acute anxiety in the knowledge that the supply of ACTH would soon become exhausted, that her disease would return with its suffering and that she would run a rapid downhill course with ultimate death. This was impossible to accept with the knowledge that a drug was available which she believed could prevent such an outcome.

After eleven months of ACTH therapy, there has been no evidence of resistance nor reactions to ACTH. It is our feeling that this patient can be maintained indefinitely in a state of well-being on ACTH in the form of replacement therapy. We have no evidence which would suggest that a cure of the disease could be obtained with this hormone.

Observation of the patient during this period makes one question the advisability of treating a chronic illness with ACTH unless one can be reasonably certain of a continued supply of the drug.

CONCLUSIONS

1. A case of pemphigus erythematosus (Senear-Usher disease) in a white female, aged 47, of 3 years' duration, showed a marked clinical and subjective improvement while on ACTH therapy only to relapse on withdrawal of the drug.

2. Cortisone in dosage used failed to produce a remission in this patient.

3. ACTH in a continuous intravenous drip produced the most rapid and dramatic clinical results with the smallest dosage.

4. ACTH in an oily preparation given intramuscularly as a single daily injection appears to be an effective method of treating such serious and debilitating diseases as pemphigus on an ambulatory basis when carefully supervised.

5. Treatment with ACTH in pemphigus apparently has to be continued indefinitely or until a spontaneous remission occurs. The treatment carries with it the risk of side effects of ACTH.

Appreciation is expressed to Miss K. Hoskins of the X-ray Department of the Vancouver General Hospital, for the illustrations.

ACTH and Cortisone were supplied by the National Research Council of Canada and adactar-0-40, Lot No. R-255136 was made available by the Armour Company through the courtesy of Dr. H. Cluxton.

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REFERENCES

1. MANDEL, W., SINGER, M. J., GUDMUNDSON, R., MEISTER, L. AND MODERN, F. W. S.: Intravenous use of pituitary adrenocorticotropic hormone (ACTH). A report of its administration in twenty-five patients, *J. A. M. A.*, **146:** 546, 1951.

CLINICAL STUDY IN MAN OF THE EFFECTS OF VARIATION OF "AGENIZED" FLOUR PRODUCTS IN THE DIET

In a detailed and critical study of white bread and cake flour which had been bleached with nitrogen trichloride (agene), no toxic effects were noted. The authors used a group of 27 children—7 to 13 years of age—who showed abnormal electroencephalograms and six controls.

No changes were noted in C.N.S., biochemical or urinary studies when agenized products were withdrawn or re-introduced into the diet.—Laufer, M. W., Denhorf, E. and Giunta, F.: *J. Pediat.*, **38:** 341, 1951.

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PHOSPHORUS SESQUISULPHIDE POISONING

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RECENTLY, two cases of dermatitis of the face due to sensitivity to friction matches were briefly reported.[1] Because of further investigation and thought, the first case of that report is again described. A second case of this kind which has given valuable information as to the etiology of the disease is now added. The ordinary type of match dermatitis as seen in males shows an eczematous dermatitis on the thighs from contact with pockets saturated with match tip material, and occasional involvement of the face is seen as a secondary phenomenon. It should be emphasized here that the cutaneous manifestations in these two cases occurring in females are the result of a primary sensitization about the eyes and face.

CASE 1

Mrs. R.B., age 61, in 1933 had a severe recurring œdematous dermatitis over a period of twelve months about the eyes and face for which a cause was not found, in spite of a good deal of investigation. At or about the same time, she developed a marked loosening of many teeth and as it was thought that pyorrhœa might be a possible cause although no caries was present, these were all extracted. Her teeth had practically no fillings and had been exceptionally good. The facial condition gradually disappeared although there occurred at times some slight dermatitis with itching about the eyes.

About 1941 she again began to get attacks of œdematous dermatitis about the eyes and face which gradually increased in severity and frequency particularly during the past four years. These attacks, which lasted five to ten days, were accompanied by prostration, a marked vertigo, loss of appetite, nausea, and vomiting, necessitating bed rest and absolute quiet. A great deal of medical and dermatological investigation over these years again failed to reveal a cause.

In March 1950, a chance remark by the patient led to the real cause being found—"I would even give up smoking if I could get rid of this". A patch test with a friction match applied to the forearm gave a rather delayed reaction but one which persisted through several weeks. With this clue, on giving up matches and using a lighter for the past year, she has been perfectly well and free from all local and systemic symptoms. She is only a very moderate smoker. Patch tests done with a safety match and with the friction side of a safety box were mildly positive in forty-eight hours.

CASE 2

Mrs. D., age 31, presented a recurring dermatitis about the eyes, of nine months' duration. There was œdema, redness, and itching about both eyes and cheeks, characterized by periods of exacerbation and quiescence. She said that at times her eyes had been itchy without any eruption over the past four years. She was a free lance professional model and this was then a real disability. Treatment had been hitherto ineffectual. She was a smoker and also was fond of striking matches, but not with her nails. A patch test in her case with a match tip gave a vesicular reaction within twenty hours. Later, separate patch tests with the tip and the blue portion of the tip were also positive, the reactions being still very evident at the end of three weeks. Patch tests also done with a safety match tip and with the friction surface of the safety box were slightly positive. She promptly cleared up on discontinuing the lighting of matches.

In the past two years she had had some loosening of both upper and lower teeth, for which condition other causes were ascribed. In the past three months since refraining from the use of matches, this process, particularly as it affected her lower teeth, has become definitely improved as verified by her dentist

She further stated that transitory attacks of dizziness had occurred at times and volunteered the information that she had often noted that sneezing occurred with the first puff of a cigarette (nasal allergy).

Dermatologists not infrequently see cases of eczematous dermatitis in females who give a history of a marked exacerbation of the inflammatory process prior to menstruation so that such cases have sometimes been ascribed to menstrual changes. It is recorded here, that in Case 2 prior to and during three successive menstrual periods, the area on her chest at the site of the original patch test became inflamed and itchy, subsiding completely in the intermenstrual period.

Further investigations and comments.—Investigation of these cases therefore has shown (1) positive patch tests with the whole match tip (containing phosphorus sesquisulphide P_4S_3 and other components); (2) positive patch tests with the ignition (phosphorus sesquisulphide) and also the burning portion of the tip (contains sulphur, potassium chlorate, and other components) probably due to traces of phosphorus sesquisulphide P_4S_3; (3) a slightly positive reaction with safety match tip (contains antimony sulphide Sb_2S_3, and an oxidizing substance); (4) slightly positive patch test with striking surface of safety box (contains red phosphorus and an oxidizing agent). The patch tests with 10% sulphur ointment were negative in each case.

That this process is partially one of contact with the fumes of burning match tips is shown by this observation. Case 2, for one day used several friction matches to light cigarettes and in twenty-four hours developed itching and a moderate dermatitis about the eyes. At a later date, when this had entirely subsided, she was asked to particularly handle the tips of friction matches for one day. In eight hours, she had developed a much more severe dermatitis about the eyes from the contact of the fingers with her eyes due to a greater concentration of the offending material. Case 1 handled the match tips for one day, but carefully kept her fingers from her eyes and no dermatitis resulted.

The tip of a friction match is made up of an igniting portion which contains phosphorus sesquisulphide together with substances which are

also present in the burning portion, namely an oxidizing agent such as potassium chlorate with combustible substances such as sulphur, paraffin, glue, and abrasives. A safety match is dipped in a readily combustible substance such as antimony sulphide Sb_2S_3 and an oxidizing agent such as potassium chlorate, whereas the striking side of the box contains red phosphorus and an oxidizing agent together with abrasives and glue.[2]

Yellow phosphorus is semi-transparent, soft and waxy, has a garlic-like odour, and is poisonous. Its use in making matches was long ago discontinued because the match factory workers developed "phossy-jaw". Red phosphorus is made from yellow phosphorus by its exposure to high temperatures in a vacuum, is more stable, oxidizes much less rapidly, and is non-poisonous. This allotropic variant is now used in the manufacture of matches in the form of phosphorus sesquisulphide P_4S_3. "When heated, red phosphorus sublimes forming vapour composed of molecules of P_4. Upon condensation of the vapour, the yellow form is produced."[2]

As an industrial hazard, apart from acute phosphorus poisoning, phosphorus absorption from fumes over a long period of time (two to five years) may result in loosening of the teeth from variable degrees of necrosis of the jaw and caries of the teeth. It is said that necrosis results in and about carious teeth, the presence of bacteria being necessary. Workers who handle phosphorus frequently develop burns and caustic lesions, dermatitis, conjunctivitis, itching, or nasal irritation. Chronic symptoms include a garlic odour, increased red and white cell count, enlarged liver followed later by jaundice, anæmia, and jaw necrosis with general prostration. (This refers to yellow phosphorus[3]).

These cases of dermatitis about the eyes and face due to contact with and hypersensitivity to the fumes of match tips and associated with loosening of the teeth and dental caries, have not been recognized and may be not uncommon. The duration in both cases was long. While direct contact with match ends may produce an acute dermatitis about the eyes when carried by finger tips, it is neither customary nor common that in the handling of such matches for lighting purposes the inflammable tip of the match is touched. Individuals for practical purposes only contact the wooden end; particularly is this true of females, who do not carry friction matches as a rule.

The cutaneous manifestations may be explained by a sensitivity to phosphorus sesquisulphide and its combustion products. On the other hand, the causes of the toxic manifestations, notably present in Case 1 and the dental changes in both cases, be they of similar origin, are somewhat more difficult to assess. It is possible that unoxidized atoms of phosphorus may be present in match combustion vapour but it would seem unlikely. Incomplete oxidation forms of phosphorus, the best known of which are the trioxide P_4O_6 and the pentoxide P_4O_{10} or of the phosphorus sulphides, could, through inhalation, give rise to slower but similar phenomena as those seen in factory workers when exposed to yellow phosphorus.

SUMMARY

Two cases of poisoning in females by the fumes of burning match tips (containing phosphorus sesquisulphide) arising over a long period of time through the daily lighting of friction matches are described. This poisoning resulted in a recurring severe primary dermatitis about the eyes and face. In each case, loosening of the teeth occurred which may have been due to phosphorus poisoning. In one case a severe systemic poisoning resulted which cleared up completely on discontinuing the use of matches. The possible means by which this systemic and cutaneous poisoning could have resulted are discussed.

REFERENCES

1. BURGESS, J. F. AND FORSEY, R. R.: Contact Dermatitis of the Face due to Matches, *Arch. Dermat. & Syph.*, In press.
2. BRISCOE, H. T.: General Chemistry for Colleges (4th ed.), Houghton Mifflin Co. (Riverside Press) Cambridge.
3. GLAISTER, J.: Medical Jurisprudence and Toxicology, E. & S. Livingstone Ltd., Eden Press, 1945.

RÉSUMÉ

L'auteur cite deux cas d'empoisonnements par le sesquisulfure de phosphore qui sont survenus chez des femmes, au cours d'une longue période de temps et à la suite de l'allumage quotidien d'allumettes ordinaires à friction; cet empoisonnement tenait aux vapeurs provenant de la combustion des bouts d'allumette enduits de phosphore.

L'intoxication exogène prit la forme d'une dermatite primitive grave située à la face et au pourtour des yeux et elle fut accompagnée dans chaque cas par un décollement marqué des dents, qui était probablement causé par une nécrose de la mâchoire directement imputable à l'inhalation des vapeurs. Dans un de ces cas, une septicémia grave fit suite à l'apparition de ces autres symptômes.

Il semble bien qu'il faille trouver l'explication de ces phénomènes dans la conversion du phosphore rouge non toxique dans les bouts d'allumettes en un phosphore jaune toxique, changement qui s'opère au cours de la combustion.

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THE RADIOLOGIST AND EPIGASTRIC PAIN*

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IN THE PAST FEW YEARS abdominal radiology has advanced in many ways. Sharper images are now produced by faster film, faster screens and higher milliampere apparatus. Spot film devices allow visibly controlled angulation which may be altered from patient to patient. These devices also allow adjustable compression of underlying tissues. The result is a much more accurate assessment of tissue abnormalties. These modern techniques have had their application further improved by better tolerated opaques for gall bladder and kidney work. Barium emulsion is also improved, so that the barium does not drop out of suspension.

None of these advances however can replace skill in their use. Variation in method of study of each individual case must still be the responsibility of the conscientious, experienced radiologist. Abnormalities of many types cannot be recorded on films without his inquisitive fluoroscopic survey. Interpretation of his findings must be determined both by abnormalities of tissue structure and abnormalities of function.

All radiologists have experienced during the past fifteen years, the tendency of referring clinicians to ask, in effect "has this patient something organically wrong in his epigastrium or are his symptoms functional in origin?" By functional they evidently mean something either non-surgical or existing in the patient's imagination only.

The above question requires answering certainly and marks an advance on the attitude of fifteen years earlier. The question at that time was, "this patient has a peptic ulcer. What chance has he of perforating, bleeding or obstructing?"

The time is coming and is now here for many clinicians to ask the right question of their radiological confrères. The question is very simple and puts the responsibility where the clinician really wants it placed. It is as follows: "This patient has pain or tenderness or discomfort in his upper abdomen. Will you try to find out for me the cause of the pain by your methods as I am not sure by my own?" The radiologist is then prepared to use any or all of his procedures to demonstrate abnormalities in any abdominal viscus. He may show functional abnormalities resulting from pathologic changes at some distance from the site of the symptoms.

The radiologist daily watches the œsophagus, stomach and duodenum function. By long observation of the normal he is taught to appreciate the abnormal. The frequency and amplitude of peristaltic action in normals is as easily and surely recognized by him as his office furniture would be. The observation of abnormalities of function or in other words functional abnormalities may be his clue to the solution of the symptom complex. The solution may be elusive and if not followed completely is unsatisfactory to the patient and clinician. It is discouraging to the radiologist. For him it is comparable to missing the last paragraph of a good murder mystery.

Some years ago we were prone to consider that if an ulcer crater or a space occupying new growth could not be demonstrated in a film we were examining a stomach which did not produce symptoms. Those days have gone forever.

We must always watch for the unusual. The multiplicity of unusual findings which can be demonstrated or strongly suspected in the upper abdomen forms a formidable group. Because of the bizarre pattern of their symptomatology these are the patients most frequently referred for x-ray studies. I am of the opinion that at least half of the patients referred for x-ray investigation of the gastro-intestinal tract and in which the more obvious lesions cannot be demonstrated will have demonstrable abnormalties of function. These demonstrable abnormalities are chiefly aperistalsis, hyperperistalsis, dilation of the lumen, spastic contractions of the lumen and marked variation in motility of the test meal. These findings are at variance with our usually appreciated causes for pain of intestinal origin. They are of course marked dilation or stretching of the bowel, tonic contractions of the bowel or ulcerative erosions of the mucosa anywhere in the gut.

We know that surgeons can enter the abdomen of a patient with infiltration anæsthesia of the wall only and cut, cauterize and suture without causing pain to the conscious patient. But traction must not be put on the mesentery. Actual palpation of an ulcer does not cause pain. When examining this patient in bed before surgery, a lot of dependence is placed on findings of deep tenderness or pain on deep pressure.

*Read at the Annual Meeting of the Ontario Medical Association, May, 1951.

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Our physiologists have plotted referred pain areas from visceral pathology and have been very helpful. There seems to be only one explanation and that is, that the area of referred pain must also be receptive to stimuli or the pain cycle is broken. The radiologist, when screening, attempts as complete manipulation of gastric and intestinal contours as relaxation and costal margins will permit. His tender spot in duodenal ulcer is over the referred area and does not descend with the duodenum when the patient is changed from the horizontal to the upright position. This area is above and to the left of the demonstrable crater. In fact the structure immediately underlying it is most often the gastric lesser curvature. This does not mean that the patient has no sense of the origin of the pain. The intelligent co-operative patient will often tell you that pressure on the referred area causes pain elsewhere and will bring his pointing finger somewhere near a spot overlying the ulcer. You have all had the same experience with appendicitis. Pain may be classically placed and the appendix inches away from the expected location.

The more fixed viscera, notably the gall bladder and iliac loop of sigmoid, present tenderness more usually in the expected area. The latter of course is probably due to easier accessibility to palpation.

Let us now return to the epigastrium. The diagnosis of cardiospasm has long been considered a very simple radiologic problem. The massively dilated œsophagus containing food and with overhang on both sides of a pencil-sized constriction of the outlet is classical. Our endoscopists have made the discovery that cardiospasm is much more common than previously suspected. The early findings may be really difficult to demonstrate, as there may be a minimum of œsophageal stretching. It may be easily missed on a hurried fluoroscopic examination. This group now includes many patients with post-cricoid fullness due to neuromuscular derangement of the swallowing apparatus. Unusual delay in transit of the meal with even questionable dilation of the œsophagus where new growth, varices and ulcer can be ruled out, must be considered cardiospasm. The neuromuscular derangement may present another area of spasm well above the hiatus. These cases deserve repeat examinations, as peptic ulcer of the œsophagus may later be demonstrated in its lower segment.

Hiatal hernia, short œsophagus and partially intra-thoracic stomach, present such a distinctive finding that it should not be missed. The so-called sliding hernia with intermittent protrusion through the hiatus, present only in Trendelenberg position or on forced inspiration or on increased abdominal pressure is seldom productive of severe symptoms. Any hiatal hernia should therefore be examined for spontaneous reduction and proved to be either sliding or incarcerated.

Another group of uncomfortable people is the air swallowers. This group may have their abnormality recognized, their symptoms explained and their condition cured by the radiologist. We often see a half glass of barium cream enter the stomach with three or four times its volume of air. We watch the cardia expand and the left diaphragm ascend. The cure of course is to tell the patient what he is doing and where the supposed gas comes from. The second glass of barium is swallowed deliberately and in small mouthfuls with a minimum of air. The intelligent patient is immediately cured. Those who swallow air during their sleep are usually free of air before they reach the department and the diagnosis is made by elimination of other causes.

The next functional abnormality to be considered is gastrospasm. I find myself reporting this phenomenon much more frequently in recent years. By gastrospasm I do not mean an incisura at or below the level of a gastric ulcer. There is an occasional stomach usually of the oblique type, high up under the costal margin, which seems to fill completely with four to six ounces of the barium mixture. The mucosal folds are heavy and close together. These stomachs can only be studied in the horizontal position with a patient lying partially on his left side. The stomach empties rapidly. The presence of peristalsis rules out linitis plastica. For want of a better term I have considered this finding as indicative of gastritis.

Spasm of the pyloric segment of the stomach is a most difficult finding to assess. On fluoroscopy, peristalsis is interrupted two or three inches proximal to the pylorus and reappears within one-half inch of the sphincter. The mucosal pattern is compressed but not grossly deformed. The gastric profile in the area may suggest new growth. There is slight or no delay in emptying time. Localized pain is present which I believe has a diagnostic value in favour

of spasm rather than new growth. Fortunately the site is accessible to palpation and the absence of tumour usually can be verified. A differential diagnosis between pure spasm and antral gastritis is extremely difficult.

To differentiate between antral gastritis with spasm and mucosal distortion and early prepyloric new growth is sometimes difficult and often endoscopy is required. Where this is not easily available exploratory laparotomies have been done for visual diagnosis. Under general anæsthesia the stomach is relaxed even if inflamed and the suggestion is put forward that an occasional stomach should be studied, fluoroscopically, barium coated under general anæsthesia.

Pylorospasm in association with peptic ulcer within the canal or close to either extremity can present considerable difficulty. The difficulty is diminished and in many cases overcome by interrupting the examination. The patient is allowed to lie down relaxed for fifteen or twenty minutes. Actual visualization of the pyloric canal is essential for diagnostic accuracy. I have not had any help in this problem from the use of antispasmodics or sedatives.

Gastrospasm in association with duodenal ulcer or gall bladder or bile duct disease is sufficiently well known as to require mention only. The typical constricted crenated caput seen in duodenitis is classical and need not be further mentioned.

There is a large group of functional stomachs presenting antral spasm or pylorospasm of sufficient moment to cause upper abdominal symptoms, in which we later find abnormalities of the colon. These abnormalities may be appendicular or cæcal. They may be diverticula of the transverse colon or sigmoid. There may be the tapered cone-shaped rectal ampulla seen in fissure or thrombosed hæmorrhoids. In many of these I have noted that the upper abdominal discomfort is the predominant symptom. Many patients are averse to inviting a rectal examination and therefore do not mention anal or rectal symptoms unless severe.

In an effort to give these examinations practical value, I feel the radiologist should not have his examination limited by the clinician. Functional abnormalities of the stomach and duodenum should be followed by a complete gastrointestinal examination in a much greater number of cases. A rectal examination may provide the clue to treatment in many cases of functional dyspepsia.

CONCLUSION

The term functional dyspepsia has been applied in many cases of gastrospasm, demonstrable radiographically. In many of these, disease has been present elsewhere in the tract or its adnexa. I suggest that more complete x-ray examinations will solve the diagnostic problem in an increasingly greater number of so-called functional dyspeptics.

SCHISTOSOME DERMATITIS IN QUEBEC*

M. J. MILLER† and E. MUNROE‡

DERMATITIS caused by schistosome cercariæ—more popularly known as "swimmer's itch", "water-itch" or "slough itch"—is known to be common in western Canada and in various parts of the United States as well as in Europe, Asia, and Africa. There have been few records from eastern North America and none from eastern Canada. The discovery of an infested area near Montreal was therefore of considerable interest, and the opportunity is taken to describe this infestation and to review briefly the epidemiology and symptomatology of the disease. The infestation in the Montreal region has apparently existed unsuspected for many years, and it is hoped that the present discussion will aid in the identification of other unrecognized areas of infestation.

The cercariæ which cause swimmer's itch are the larvæ of blood flukes similar in most respects to those which give rise to the human schistosomiases in various parts of the tropics and the Far East. The adults are minute, dioecious flatworms, which live in blood vessels—chiefly those of the intestine—of warm-blooded animals, either mammals or birds. There are many species of these worms, but the life cycle of all is similar in outline (Fig. 1). The female

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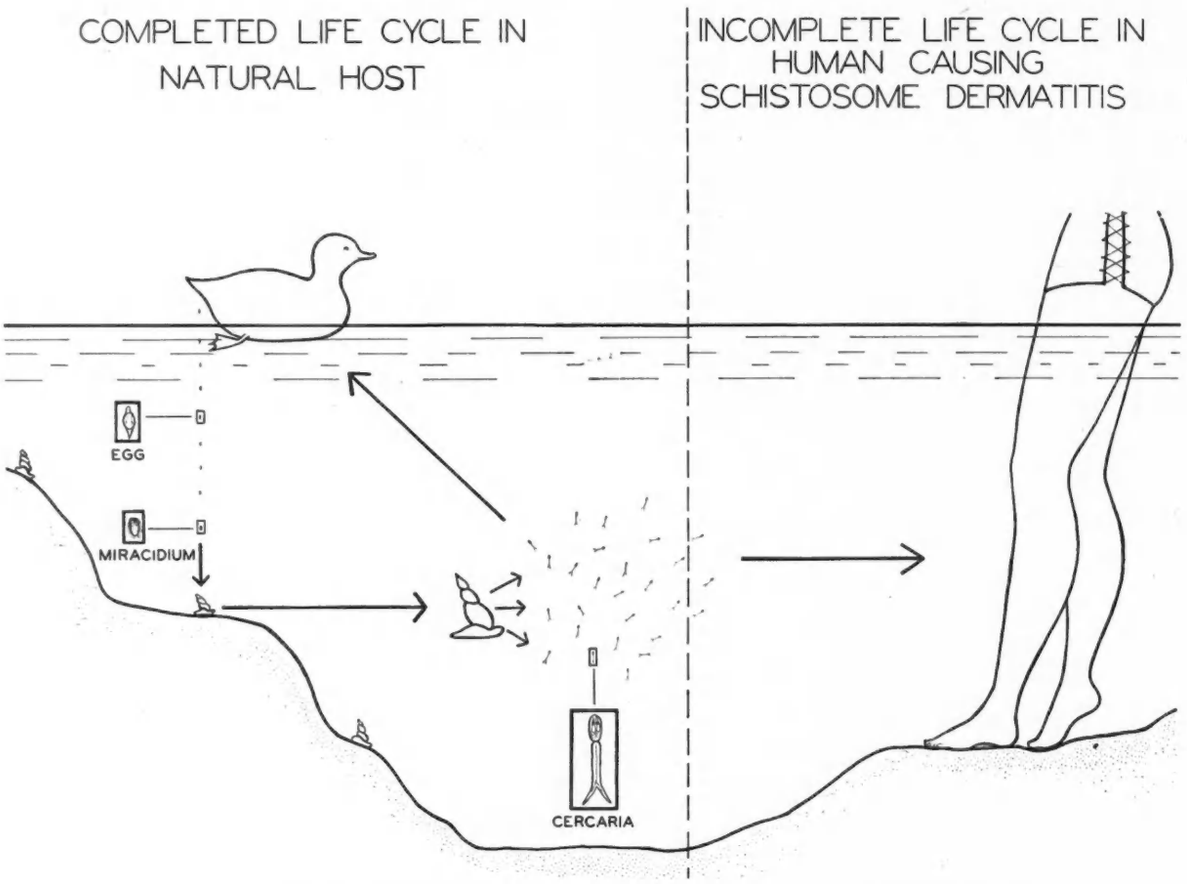

Fig. 1.—The life cycle of the parasite causing "swimmer's itch": the completed cycle with the development of the adult parasite in the natural host, and the incomplete cycle in man with the death of the cercaria and the development of swimmer's itch.

lays eggs in the tissues of the host in such a way that they work their way into the lumen of the alimentary or the urinary tract. The eggs are passed to the exterior and, if they fall into water, hatch almost immediately, yielding a ciliated *miracidium* larva. If this larva is to survive, it must within a few hours find and penetrate a suitable intermediate host, which is always a species of snail, different for the different schistosome species. Within the snail, the miracidium undergoes a complex asexual multiplication, with the result that there is eventually a daily production of hundreds of a new kind of larva, the *cercaria.* These are usually liberated at a certain period of each day; the large daily production may continue for months, so that a single miracidium gives rise to many thousand cercariæ, each one a potential adult worm.

The cercariæ leave the snail and swim actively in the water by means of a strong, forked tail. They can survive for one or two days in the free state. If during this period they encounter a swimming or wading warm-blooded animal they may penetrate the skin, shedding the now useless tail in the process. In a suitable host the young worms are carried in the blood stream, usually to the lungs, and later to the blood vessels of the intestine or other organs, where they become mature.

None of the schistosomes known in North America can complete its development in man; the cercariæ of several species, however, may penetrate the human skin, after which they die. This penetration and death is the cause of cercarial dermatitis.

Epidemiologically, the presence of swimmer's itch as a clinically important entity depends on the geographical and temporal coincidence of four factors: the parasite, a suitable intermediate host, a suitable definitive host, and a locality where humans normally come in contact with the water, by wading, swimming, fishing, etc. Due to the necessity for this combination, and probably due also to the fact that the etiology of schistosome dermatitis often remains unrecognized, our records of the distribution of swimmer's itch are

rather scattered although the causative schistosomes appear to be of general occurrence throughout North America.

Cercarial dermatitis in North America is most frequently caused by a group of schistosomes, *Trichobilharzia,* whose definitive hosts are birds, especially wild ducks; however, there is also another and epidemiologically distinct group, *Schistosomatium,* which matures in mammals, particularly rodents. These groups differ not only in host relationships, but also in geographical distribution, and in the diurnal and to some extent the seasonal periodicity of the cercariæ. The mammalian hosts of *Schistosomatium* are nocturnal, and the emergence of their cercariæ is correspondingly nocturnal. Brackett (1940) points out that such cercariæ may give rise to dermatitis chiefly among those who swim in the evening or at night, whereas the cercariæ of the avian schistosomes emerge in the morning, and may continue to attack swimmers throughout the day and evening. Due to the relationship of the migratory cycle of the avian definitive host to the midsummer dying out of the molluscan intermediate host, the incidence of dermatitis caused by bird schistosomes tends in most localities to be restricted to the early part of the summer. The mammalian schistosomes, whose hosts do not migrate seasonally, are likely to have a less restricted seasonal occurrence.

Both groups are widely distributed in North America, but apparently occur in greatest numbers in the middle west. Mammalian schistosomes have not been recorded from Canada, having apparently a more southerly distribution than avian schistosomes, which occur in many parts of the Dominion. From the three aspects of geographical distribution, abundance, and diurnal periodicity, then, the avian schistosomes are the more important group from the standpoint of dermatitis production in Canada.

Clinically, schistosome dermatitis is characterized by skin lesions which vary from a simple erythema, to large papules, red and extremely itchy. The disease follows a characteristic pattern but its severity varies from case to case. Typically there is an initial prickling sensation during exposure in the water; this coincides with the penetration of the cercariæ into the skin. Following the initial prickling, within 5 to 10 minutes small red macules appear, each one indicating the penetration site of a cercaria. These areas usually increase somewhat in size over the next several hours and may become quite itchy; in severe cases there may be a generalized blotchy erythema over the entire affected part. In any case the initial rash almost invariably subsides within 12 hours, to reappear within the next 6 to 12 hours as a papular rash which is extremely itchy. The papules increase in size for two or three days. the itching increases progressively. In some cases the papules may develop an erythematous areola and in severe cases the entire affected part becomes œdematous and tender. Not infrequently the papules become secondarily infected due to scratching, with the development of pustules and crusting.

The rash usually starts to subside by the fifth day and within a week may entirely disappear. Olivier (1949) has recently shown that schistosome dermatitis is a sensitization phenomenon, which explains the variations in severity of the disease shown by different individuals. He has demonstrated experimentally that initial exposures to infection will not result in a dermatitis and that only after a person is sensitized will he develop a rash, the severity of which is often directly proportional to the number of exposures. Undoubtedly, there is an individual element influencing severity of symptoms as well.

It is normally impossible to find the cercaria in or on the skin, so that final diagnosis must rest on the demonstration of cercariæ in waters to which the patient has been exposed. Even this cannot be done directly, as the delicate larvæ are destroyed by filtering or straining procedures. Instead, snails must be gathered from the suspected locality, and kept alive to see whether they are liberating cercariæ. Fortunately, this is relatively easy to do. The usual host species are large, spired, non-operculate snails of the genera *Limnæa, Stagnicola,* and *Physa* which are easily seen and picked up in shallow water. The large, flat ram's-horn snails, or those with an operculum (*i.e.,* a trap door which fits over the aperture of the shell when the snail withdraws into it) are not likely to harbour schistosome cercariæ.

The living snails should be placed in tap water in open wide-mouthed bottles of reasonable size—quarter- or half-pint cream bottles are satisfactory for the purpose—and five or six snails can be kept in each bottle. A parasitized snail will usually within twenty-four hours have liberated a large number of cercariæ, which can

be seen as minute, intermittently wriggling, translucent organisms when the bottle is held up to the light.

Many kinds of cercariæ may be found in snails but those of the schistosomes belong to a group which is easily recognized under the microscope by the fact that the tail is forked. Not all fork-tailed cercariæ, however, are schistosomes. The fork-tailed cercariæ are subdivided according to whether or not there is a bulbous muscular pharynx on the œsophagus. Cercariæ with a pharynx are not schistosomes; schistosome cercariæ always lack the pharynx. This character is hard to observe, as the pharynx is at best inconspicuous, but fortunately in North America it can be supplemented with a fair degree of accuracy by a more easily seen character: the presence or absence of eye spots. Pharyngeal fork-tailed cercariæ usually lack eye spots, while a-pharyngeal ones, including schistosomes, have a pair of conspicuous dark eye spots near the middle of the body.

More precise identification depends upon recognition of the host snail, and on the observation of the cercariæ in life. Living, parasitized snails should, therefore, be sent to experts if complete identification is desired.

The infestation in the Province of Quebec is an excellent example of how areas of cercarial dermatitis may be overlooked unless attention is specifically directed to them. In the early summer of 1949 a local physician reported a number of cases of a skin rash occurring in persons bathing in the Ottawa River at Ste. Anne de Bellevue, within a mile of the Institute of Parasitology. Subsequent inquiry among residents of the area indicated that a similar rash had been of regular occurrence for at least the past fifty years, though more prevalent in some years than in others, and being evident chiefly in the month of June.

Investigation of the locality revealed moderate numbers of two species of *Stagnicola* and a species of *Physa*, as well as several other species of snails. Schistosome cercariæ were immediately recovered from the *Stagnicola* and *Physa*, the incidence being about 10% in the *Stagnicola* species, and lower in the *Physa*. Experimental infection of birds showed that the cercariæ from *Stagnicola* belonged to a species of *Trichobilharzia*, whose identity is still under study.

At first none of the workers who handled the cercariæ developed a dermatitis, but within a few days one laboratory assistant proved to be susceptible, developing the rash on the hands (Fig. 2). The course of infection was then followed experimentally in this same person. Three cercariæ in a drop of water were placed on the dorsum of the hand, and within two minutes there was a prickling sensation on the infected area. By the time the water had dried there were three erythematous spots about 0.5 mm. in diameter; these were itchy and persisted for several hours but then gradually disappeared. By the next morning, however, three red and itchy papules were present. The papules gradually increased in size until they were about 5 mm. in diameter. They were constantly itchy, and no relief was obtained by the use of iodine, alcohol, ether, or of a proprietary remedy containing calamine, chloroform, menthol, camphor, and alcohol. The itching was more noticeable at night. The papules persisted for about seven days, but by the fifth day they began to decrease in size and became less itchy.

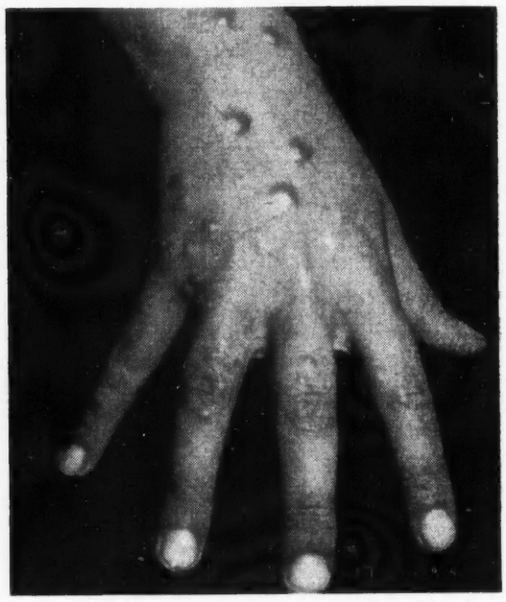

Fig. 2.—Papular eruption typical of swimmer's itch, five days after infection.

No very satisfactory control for dermatitis-producing schistosomes has been developed. There is no repellent in use which can be applied to the skin to give protection against the cercariæ. Vigorous rubbing of the body with a towel immediately on leaving the water will destroy many of the cercariæ before they penetrate the skin.

Full control can theoretically be achieved either by barring the definitive hosts (aquatic or

sub-aquatic birds, and sometimes small mammals) from bathing areas or by destroying the intermediate hosts (snails). The exclusion of birds and mammals from bathing areas presents obvious and often insuperable difficulties. Snail control is also extremely difficult, though considerable reduction can sometimes be achieved by hand-picking. Copper salts have often been recommended for killing snails, and in the hands of some investigators have apparently yielded good results. However, unless used with caution, copper sulphate, which is the copper salt most frequently used, may cause damage to the fish. Frequently the most simple solution is in the exclusion of bathers from the infected areas.

BIBLIOGRAPHY

1. BRACKETT, S.: *Am. J. Hyg.*, **31(D)**: 64, 1940.
2. CORT, W. W.: *Am. J. Hyg.*, **23**: 349, 1936.
3. *Idem*: *Am. J. Hyg.*, **52**: 251, 1950.
4. CORT, W. W. AND TALBOT, S. B.: *Am. J. Hyg.*, **23**: 385, 1936.
5. MCMULLEN, D. B. AND BEAVER, P. C.: *Am. J. Hyg.*, **42**: 128, 1945.
6. MCMULLEN, D. B. AND BRACKETT, S.: *Am. J. Trop. Med.*, **21**: 725, 1941.
7. *Idem*: *Am. J. Hyg.*, **47**: 259, 1948.
8. OLIVIER, L.: *Am. J. Hyg.*, **49**: 290, 1949.

RÉSUMÉ

La dermatite causée par le schistosome cercariae, mieux connue sous le terme de "démangeaison des nageurs" est habituellement rare dans l'est du pays et plus commune dans l'ouest, c'est pourquoi la découverte récente d'une zône d'infestation aux environs de Montréal, longtemps insoupçonnée, ajoute de l'intérêt à cette question.

Cliniquement cette dermatite offre des lésions cutanées variant de l'érythème simple à de grosses papules rouges et extrêmement prurigineuses. Typiquement il existe une sensation de prurit initiale durant le contact à l'eau; cela coïncide avec la pénétration des cercariae dans la peau. L'éruption commence à s'amender vers le cinquième jour pour disparaître en une semaine.

Cette dermatite est un phénomène de sensibilisation. Il a été prouvé en effet qu'un contact initial ne résulte pas en une dermatite, et ce n'est qu'après qu'un individu a été sensibilisé qu'il verra apparaître l'éruption.

Il n'est guère de mesures prophylactiques contre cette infection, si ce n'est que de détruire totalement tous les colimaçons, qui semblent être les hôtes intermédiaires les plus usuels. Cependant, un vigoureux frottage du corps avec une serviette rude immédiatement après la sortie de l'eau détruira presque tous les cercariae avant qu'ils ne pénètrent la peau.

THE LARYNGEAL SWAB SPECIMEN IN THE CULTURAL DIAGNOSIS OF PULMONARY TUBERCULOSIS

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FOR A NUMBER OF YEARS it has been accepted sanatorium practice to culture gastric aspirations when investigating patients without sputum, or whose sputum has been culturally negative for tubercle bacilli on previous occasions. The gastric specimen has been shown by several investigators to be superior to other material. Results of studies conducted in this laboratory in 1939[1] were in agreement with this contention. The value of the procedure is limited by the discomfort occasioned to the patient and the time taken to obtain the specimen.

As early as 1905, Blume[2] used laryngeal swabbing to obtain material for direct smear examination for acid fast bacilli. Subsequently Grass,[3] 1931, employed laryngeal swabbing with success for cultural diagnosis in open cases of tuberculosis. Later Dornickx,[4] 1937, Benzançon *et al.*[5] 1937, Böhm and Ekstein,[6] 1938, obtained satisfactory results in patients who did not expectorate. The first report in English on the subject was that of Nassau,[7] 1941, who was able to secure a high percentage of positive cultures from patients discharged from a sanatorium in England. The method was studied by Hounslow and Usher,[8] 1948, who actually compared the laryngeal swab specimen with gastric lavage and concluded that the results of three consecutive laryngeal swabs are as good as, and probably better than, a single gastric lavage. Simultaneously Forbes *et al.*,[9] 1948, reached similar conclusions. In Canada, Duggan and Delamater,[10] 1950, compared gastric specimens with laryngeal swabs in 100 consecutive cases and concluded that two, or preferably three cultured swabs are as accurate as a single gastric lavage. All investigators have been unanimous in concluding that the swabbing procedure is less unpleasant for the patient and an easier one for the technician.

The English publications, together with discussions with several visiting British phthisiologists, aroused our interest in the subject. We were skeptical of the results, since we were not entirely satisfied that the techniques employed for handling the gastric lavage by the other investigators were the best available, and might therefore produce fewer gastric positive cultures than we would have obtained. It is well known that some gastric juices are lethal to tubercle bacilli, particularly when the material is not refrigerated or neutralized immediately. The practice in this institution has been to receive the lavage material directly into tri-sodium phosphate,[11, 12, 13] which preserves the viability of the organisms, and it was felt that, in some instances where this was not done, there may have been loss in viability. If this was the case it would give an apparent advantage to laryngeal swab specimens, since in them there is no gastric juice to kill the organisms.

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It also occurred to the author that the laryngeal swab would be particularly well adapted to fluid culturing, since the amount of sediment involved would be very small and that conversely it might be possible to show the swab up even more favourably. It was, therefore, decided to reassess the value of the swab specimen by comparing 1,000 cultured fasting gastric juice samples with 1,000 triplicate laryngeal swab specimens subjected to liquid culturing. The swabbing was to be done in triplicate, since other investigators had mentioned the figure of three laryngeal swabs for each gastric. The value of the swab at a chest clinic was also considered worthy of study.

MATERIAL

The lavage material and the swabs for the comparisons were secured from patients for whom gastric lavage had been ordered as a hospital routine. On the morning of the lavage a swab was also taken. Two other swabs were made: one on a day prior to gastric lavage; another on a day after. As a rule these swabs were done within one day of the lavage, but in some instances the time was somewhat greater. It was never longer than three or four days, the entire collection being completed within seven days.

While the laryngeal swab taken on the day of the gastric lavage was obtained in the fasting state, no effort was made to do this with either of the other two swabs taken. Sometimes they happened to come before breakfast, but at others they were secured at different periods of the day.

In all, 1,024 comparisons were set up and this report deals with 967 of these which were brought to completion without contamination having occurred in the lavage cultures or in any one of the three laryngeal cultures (49 laryngeal swab cultures out of a total of 3,072 were contaminated—1.6%).

These 967 comparisons (967 gastric lavages; 2,901 laryngeal swabs) were done on a total of 475 patients. Of these patients, 178 were used for comparison tests once, 183 twice, 65 three times, 30 four times, 11 five times, 6 six times, 1 seven times and 1 ten times.

In addition to the comparison study, 530 swabs were taken on 489 chest clinic patients who were suspected of having tuberculosis, or who were known to have had tuberculosis formerly.

TECHNIQUE

The entire fasting gastric contents were aspirated into an ounce of 10% tri-sodium phosphate (23% $Na_3PO_4.12 H_2O$). On receipt in the laboratory, more tri-sodium

TABLE I.

A COMPARISON OF THE RESULTS OF CULTURING GASTRIC LAVAGE AND TRIPLICATE LARYNGEAL SWAB SPECIMENS, ALL TAKEN WITHIN A PERIOD OF ONE WEEK

	Swab No. 1	*Swab No. 2*	*Swab No. 3*	*Swab Nos. 1 and 2*	*Swab Nos. 2 and 3*	*Swab Nos. 1 and 3*	*Swab Nos. 1, 2 and 3*
Gastric − swab −	804	812	814	775	778	788	763
Gastric + swab +	56	67	67	77	77	83	84
Gastric + swab −	43	32	32	22	22	16	15
Gastric − swab +	64	56	54	93	90	80	105

The figures in the first three columns refer to the number of comparisons between the gastric and the particular swab indicated at the column head. In the case of the other columns, they refer to comparisons between the gastric and the group of swabs shown at the column head, any one positive swab constituting a positive for group.

TABLE II.

A SUMMARY OF TABLE I.

	Swab No. 1	*Swab No. 2*	*Swab No. 3*	*Either or both of swabs 1 and 2*	*Either or both of swabs 2 and 3*	*Either or both of swabs 1 and 3*	*Any one, two or all three swabs*
Gastric + regardless of what the swabs were	99	99	99	99	99	99	99
Swabs + regardless of what the gastrics were	120	123	121	170	167	163	189

These figures refer to the number of positive gastrics or swabs found when the particular swab or group of swabs indicated at the column head were studied, any one positive swab constituting a positive for the group.

phosphate was added, if necessary, to make equal volumes of it and specimen. After 24 hours' incubation at 37°, centrifugation, neutralization of the sediment, the latter was planted on two tubes of Petragnani's medium.[13]

A detailed description of the technique of making and culturing the laryngeal swab has been published elsewhere,[14] but very briefly it consisted of attempting to enter the larynx with a moistened laryngeal swab, at which time the patient coughed on the swab or in some instances had to be asked to cough. The technique obviously constituted a hypopharyngeal swab except in rare instances when the larynx is actually entered. But the misnomer is good in that it keeps before the operator an objective which, when striven for, ensures that a good specimen is secured. The swab was treated with tri-sodium phosphate over night and the neutralized tri-sodium phosphate solution and digested secretion added to a quantity of liquid oleic acid-albumin medium.[15] It was incubated and examined weekly for eight weeks, or until growth had occurred, when it was subcultured to solid medium for confirmation of colony identification. In most instances colony identification was definite in the liquid medium itself.

RESULTS

In 204 of the 967 completed comparisons, tubercle bacilli were grown from either or both the gastric lavage or one of the triplicate swabs. The summarized results are presented in the accompanying Tables I and II. From these it can be seen that even single swabbings were consistently conducive to the finding of more positive cultures than single gastric lavages. Two swabbings were definitely superior to single lavages; three resulted in almost doubling the positive cultures found. Swab No. 2, which was always taken in the fasting state prior to the lavage, was not significantly better or worse than the others. In Table III are shown the findings when comparisons were repeatedly made on one patient. The superiority of the swab is again evident.

TABLE III.

TEN COMPARISONS BETWEEN CULTURED GASTRIC LAVAGE AND TRIPLICATE LARYNGEAL SWABS TAKEN FROM THE SAME PATIENT

Date	*Gastric*	*Swab No. 1*	*Swab No. 2*	*Swab No. 3*
19/6/50	—	+	+	+
26/6/50	—	+	+	+
10/7/50	+	—	—	+
13/7/50	—	+	+	+
22/7/50	—	+	—	+
2/10/50	+	+	+	+
5/10/50	—	+	—	+
12/10/50	—	+	—	+
20/10/50	—	+	+	+
26/10/50	+	—	+	+

Both patients and technicians were in agreement that swabbing is much less of an ordeal than lavaging. However, in the case of children who will not co-operate, it was felt that, if the operator was experienced at lavage, it was still the method of choice, since with a struggling child the swab is of necessity heavily contaminated with mouth secretion.

With regard to the study at the chest clinic, culture demonstrated 15 cases to be bacillary. (Nineteen swabs were positive). The procedure was found well adapted to chest clinic work, and the Director and staff of the clinic were enthusiastic about it. An estimate of the cost of taking and culturing a single swab when large numbers are being routinely processed gave a figure of approximately $1.75. Thus, based on the incidence of the number of positives detected at this clinic, routine swabbing with a similar patient clientele would cost approximately $57.00 for every case found positive. This seems reasonable enough from a public health point of view.

SUMMARY AND CONCLUSIONS

967 comparisons were made between cultured gastric lavage and cultured laryngeal swab specimens taken from sanatorium patients routinely being subjected to gastric lavage.

For each lavage performed triplicate swabs were taken, one on the day of lavage and one on each of a day before and after it, all being completed within a week. The swabs were treated with tri-sodium phosphate and cultured in liquid oleic acid-albumin medium.

Results indicated that under these conditions one swab was a somewhat superior specimen to one lavage; three consecutive swabs were almost twice as valuable in yielding positive cultures as one lavage.

The procedure of swabbing is much easier on the patient and less time consuming for the staff. It is of value at a chest clinic.

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REFERENCES

1. STANBURY, W. S. AND ROBABECK, C. H.: Unpublished data presented at the spring meeting of the Ontario Laennec Society, 1940.
2. BLUME, C. A.: *Hospitalstid.*, 13: 557, 1905.

3. GRASS, H.: *München. med. Wschnschr.*, **78**: 1171, 1931.
4. DORNICKX, C. G. J., *Nederl. Tijdschr. v. Geneesk.*, **81**: 3553, 1937.
5. BEZANÇON, F., BRAUN, P. AND MEYER, A.: *Bull. Acad. Méd.* Paris, **117**: 506, 1937.
6. BÖHM, F. AND EKSTEIN, A.: *Beitr. klin. Tuberk*, **92**: 77, 1938.
7. NASSAU, E.: *Proc. Roy. Soc. Med.*, **34**: 397, 1941.
8. HOUNSLOW, A. G. AND USHER, G.: *Tubercle*, **29**: 25, 1948.
9. FORBES, G. B., SMITH, B. J. D., HURFORD, J. V. AND SPRINGETT, V. H.: *Lancet*, **2**: 141, 1948.
10. DUGGAN, M. AND DELAMATER, L.: *Canad. M. A. J.*, **62**: 54, 1950.
11. CORPER, H. J. AND STONER, R. E.: *J. Lab. & Clin. Med.*, **31**: 1364, 1946.
12. ARMSTRONG, A. R.: *Canad. M. A. J.*, **59**: 73, 1948.
13. ARMSTRONG, A. R. AND SMITH, P.: *Canad. J. Med. Tech.*, **11**: 20, 1949.
14. ARMSTRONG, A. R. AND FOSTER, E. D.: *Canad. J. Med. Tech.*, **13**: 108, 1951.
15. DUBOS, R. J. AND MIDDLEBROOK, G.: *Am. Rev. Tuberc.*, **56**: 334, 1947.

THE CONSERVATIVE TREATMENT OF SINUSITIS*

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THE SIGNS AND SYMPTOMS of acute and subacute sinusitis are so indefinite at times that the infection is often not recognized in the early stages. This is particularly true in children where a postnasal discharge is frequently neglected. Early treatment in these cases would prevent many of them from becoming chronic.

The press and radio suggest cures for sinusitis and at times the family physician mentions "sinus" as the cause of almost any type of headache complained of by the patient. Practically every day rhinologists are consulted by patients complaining of "sinus headaches" when in the vast majority examination shows that the sinuses are free of infection. It has been estimated that of all the various causes of headache less than 5% are due to disease of the nasal sinuses.

The sinuses are air spaces which are outgrowths from the nasal mucous membrane. These evaginations eventually hollow out the bones of the skull and the sinuses thus formed are named after the bones which are invaded. The sinuses or air cavities are variable in number and are divided roughly into an anterior and posterior group. The anterior group are those that open into the middle meatus and comprise the antrum, frontal sinus and anterior ethmoid cells. The posterior group are the posterior ethmoid cells which open into the superior meatus and the sphenoid sinus which opens above and behind, in the sphenoethmoid recess. In other words the anterior group develop from the nasal mucous membrane below the attachment of the middle turbinate and the posterior group from the mucosa above the middle turbinate.

At birth the maxillary antrum and ethmoid cells are present but the frontal and sphenoid sinuses have not yet appeared. The antrum, the sinus most frequently involved in sinusitis, develops early in the fetus and resembles a small bean at birth. It reaches its maximum size about the fifteenth to eighteenth year but is of clinical importance at all ages of childhood and adult life.

The ethmoid cells are nearly all present at birth and occupy their permanent relative position. They vary greatly in number in different individuals. The cells which are formed from the mucous membrane of the middle meatus lie anterior to those which are derived from the superior meatus. Five to ten cells comprise the anterior group and two or three the posterior. These cells grow rapidly and attain their full growth between twelve and fourteen years of age. They are frequently involved in childhood.

The frontal sinus is not present at birth. Within the first few years one of the anterior ethmoid cells invades the frontal bone and at the end of the fourth year the sinus is about the size of a pea. It has little or no clinical significance until the seventh or eighth year.

The sphenoid sinus is not recognizable at birth. A pouch of nasal mucous membrane is present but it has not yet invaded the cartilage or sphenoid bone. During early childhood this cell grows slowly and it does not develop to any extent until the twelfth to the fifteenth year. As a result the sphenoid does not present a problem in early childhood compared with the other sinuses.

In infancy the sinuses are simply outgrowths of the nasal mucous membrane. Therefore infections such as acute rhinitis which affect primarily the nasal mucosa also involve the sinuses. When the acute inflammation in the nose clears up, as a rule the coexisting infection in the sinuses subsides. In childhood the sinus openings are relatively large but as these cavities develop, the openings or ostia become small as compared to the large sinuses. This disproportion in size increases the amount of work necessary for the cilia of the various sinuses to remove infection. This is particularly true of the antrum and sphenoid where the openings are near the roof and are therefore poorly placed for drainage. In spite of this handicap, the millions of closely-packed cilia work efficiently and cleanse the sinuses. They move the overlying travelling belt of mucus which replaces itself over the antral mucosa every 15 to 20 minutes in a healthy individual, and keeps it free of infection.

The antrum is the largest of the sinuses and by far the one most frequently infected. At five years of age it has an average capacity of 5 c.c. and in the adult a large maxillary sinus often holds an ounce or 30 c.c. of fluid or pus. It has been estimated that over half the cases of sinusitis are due to an infection in the antrum. This might be explained by the fact that in a general infection involving the anterior group of sinuses, the openings of the frontal and anterior ethmoid cells open close to the ostium of the antrum in

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(A short movie in colour on Nasal Cilia was also shown.)

the middle meatus. Infection in the frontal and anterior ethmoid sinuses tends to clear rapidly due to dependent drainage but pus from these sinuses often drains directly into the antrum which acts as a reservoir. Swelling of the ostium due to infection favours retention of secretions and stagnation with the well known symptoms of sinusitis.

There is very little known regarding the function of the sinuses. For nearly two generations the standard text books have mentioned that the sinuses warm and moisten the inspired air, they act as resonators for the voice and also lighten the bones of the skull. In view of our added knowledge of nasal physiology it is difficult to accept these theories.

Recently Proetz[1] has suggested that the sinuses are developmental accidents without any definite function. They are formed, he assumes, as the bones of the face enlarge and grow away from the cranium, which is relatively stationary. As the maxilla grows outward and downward in order to support the developing alveolar process, the nasal mucous membrane is "sucked in" and lines the cavity thus formed. This would explain the position of the small ostium high up on the medial wall of the antrum. In the same way the frontal sinus appears as the heavy outer table of the frontal bone grows away from the thin stationary inner table. This seems a likely theory considering how constant the sinuses are and when they make their appearance.

The signs and symptoms of acute and subacute sinusitis are so well known that repetition is unnecessary. However, a few clinical points might be mentioned.

Acute sinusitis is usually secondary to an upper respiratory infection. It has been estimated that over 90% follow acute rhinitis and perhaps 5 to 8% are dental in origin. The anterior group of cells is much more frequently involved than the posterior. Of these the maxillary sinus, as mentioned is the one most often affected, due to its exposed position, the liability of a spreading infection from the frontal and anterior ethmoids, the exposure to dental infections, and above all the poor drainage. The anterior ethmoid cells are affected less often and the frontal sinus the least of this group.

The symptoms of acute rhinitis and acute sinusitis are so similar that often the sinusitis is not recognized. As a result every acute head cold should be considered as a potential case of sinusitis. A number of factors determine whether a simple cold subsides in ten days to two weeks or whether it localizes in one or more of the sinuses. The distribution and position of the sinuses, the susceptibility of the individual to colds, local and general immunity and the offending organism all play a part.

Symptoms which often suggest sinus involvement during an acute "cold in the head" are (1) localized pain or "neuralgia" in the region of the affected sinus, (2) tenderness on pressure due to the inflamed mucosa, (3) intermittent discharge of mucoid material or pus and (4) intermittent obstruction on the affected side.

The diagnosis is usually not difficult if pus is present and is unilateral. Cultures should be taken if possible because a great proportion show hæmolytic streptococci or pneumococci and these respond quickly as a rule to the antibiotics. (It might be mentioned that penicillin is more effective than the sulfonamides especially if anaerobic organisms are present.) Smears show the presence of neutrophils and organisms and if allergy is responsible a preponderance of eosinophils.

Transillumination is useful in comparing the antra and two frontal sinuses but is of no use for the other sinuses. In children its scope is limited, as the thin bones of the antra often transmit the light too brightly, even when filled with pus. A dull light which just shows through the bones usually gives more information than intense light.

X-ray is of much greater value although it is not necessary as a rule in making the diagnosis of acute sinusitis. The nasopharyngoscope has been a great advance as the various ostia can be examined to determine the source of infection.

The prognosis in cases of acute and subacute sinusitis is usually excellent. The vast majority when properly treated by conservative methods subside without leaving any after effects and relatively few become chronic.

It has been estimated that if acute sinusitis were recognized and treatment instituted early, at least 75% would clear up entirely. Resolution usually occurs in from one to three weeks but at times if obstruction to the sinus openings is not relieved, healing may be delayed for three or four months.

TREATMENT

Ventilation and drainage are of paramount importance. An attempt should also be made to

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prevent the growth of bacteria, to alleviate pain or discomfort, to control blood-stream infections and to avoid complications. General treatment consists of bed rest in a properly ventilated room (70 to 72° F.) with a humidity of 45 to 50 degrees if possible. Some anodyne should be given to control the pain and perhaps short wave given or an infra-red lamp used for twenty minutes at a time.

Adequate doses of the sulfa compounds may help but usually penicillin intramuscularly is more effective. Some mixed infections respond better to a combination of penicillin and dihydrostreptomycin than either one alone. Penicillin is effective against Gram-positive organisms and Gram-negative diplococci; dihydrostreptomycin broadens the anti-bacterial spectrum as it includes many Gram-negative bacteria. Given once or twice a day 0.5 gm. of dihydrostreptomycin seems to enhance the effectiveness of 400,000 units of penicillin with little likelihood of affecting the cochlear nerve. (Recently a number of cases have been reported in which dihydrostreptomycin caused an impairment in hearing which appeared to be permanent. In view of this it is questionable whether there is any advantage in giving dihydrostreptomycin over the older form of streptomycin.) The newer antibiotics such as aureomycin, chloromycetin and terramycin are often indicated when penicillin is of no avail. Although they have a greater coverage, their action is perhaps weaker and the side effects such as nausea and often diarrhœa when aureomycin is given by mouth have to be considered. Usually chloromycetin and terramycin are much better tolerated.

Locally, vasoconstrictors are helpful in shrinking the swollen turbinates. Ephedrine sulphate ½ or 1% in saline with a pH of 5.9 is one of the most effective, and is quite innocuous when used judiciously. Instilled by means of a dropper with the head over the side of the bed or in the lateral head low position, the solution reaches the sinus openings better than when used in an atomizer. Inhalations of medicated steam also help to relieve the congestion and supply moisture to the inflamed membrane.

As an adjunct to the usual forms of office treatment a weak solution of cocaine applied to the sinus ostia is very soothing to the patient.

℞ Cocaine alkaloid ..... gr. IX
Benzole (C.P.) ..... m XXX
Ol. Levand. ..... m X
Ol. Pini Sylvest. ..... m XV
Green Colour ..... qs
Liq. Petrolati ..... ad ℥ II

After shrinking the swollen membranes a pledget of absorbent saturated in the above solution and placed in the middle or superior meatus, at least makes the patient feel more comfortable for an hour or two. As a rule greater relief is obtained if the patient is given an infra-red treatment while the pack is in place.

If the middle turbinate on the affected side is crowded against the lateral wall a simple fracture toward the midline helps to promote drainage. This can be done in the early stages when the acute infection is at its height without any harmful results.

Locally, sulfa compounds or penicillin are of little value. Medicated drops remain such a short time in the nose that it is useless to expect any bactericidal effect from them; besides, the high alkalinity of the sulfa drugs tends to exert a caustic action on the nasal mucosa.

In the case of the antrum the acute stage usually subsides in a week or ten days. If the discharge continues and perhaps becomes thick and curdy, the antrum should be irrigated. Fullness and pain in the cheek are symptoms of retained secretion. Whether the washing is carried out through the natural opening or in the inferior meatus is a matter of choice. Often one or two irrigations twice a week are sufficient and the patient should be told that the opening under the inferior turbinate closes within a few days. Unfortunately, many patients have the feeling that once the antrum is opened further treatment is usually necessary.

Often a patient is apprehensive if repeated irrigations of the antrum are necessary. Also it is sometimes difficult or impossible to reason with children. A self-retaining catheter is of great value as the one opening is sufficient. From time to time various catheters have been described but are rarely seen in instrument catalogs.

Once a large opening is made beneath the inferior turbinate, either under local in an adult or general anæsthetic in a child, it is a simple matter to insert the catheter on the obturator. Irrigations are carried out by means of an adapter when necessary or the patient can insert a dropper in the catheter himself. Ephedrine or medicated drops can then be instilled as often as required.

By this means repeated punctures are avoided and patients easily tolerate the tube. When not in use the free end of the catheter is curled just inside the nostril and is out of sight. A tube such

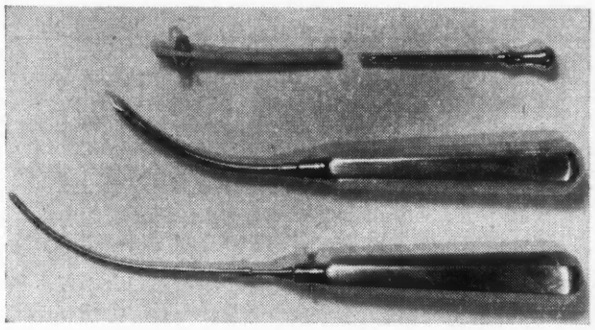

Fig. 1.—The instrument in the centre makes the initial puncture under the inferior turbinate. A Malecot 4 wing catheter Fr. No. 12 is stretched on the introducer (lowest instrument) and is immediately inserted through the perforation. The introducer is then withdrawn which causes the wings to open, holding the catheter in place. The adapter in the upper right corner with rubber tubing attached is fitted to the catheter and the antrum irrigated as often as required.
These instruments are manufactured by Storz Instrument Co., 4570 Audubon Ave., St. Louis, 10, Mo., U.S.A.

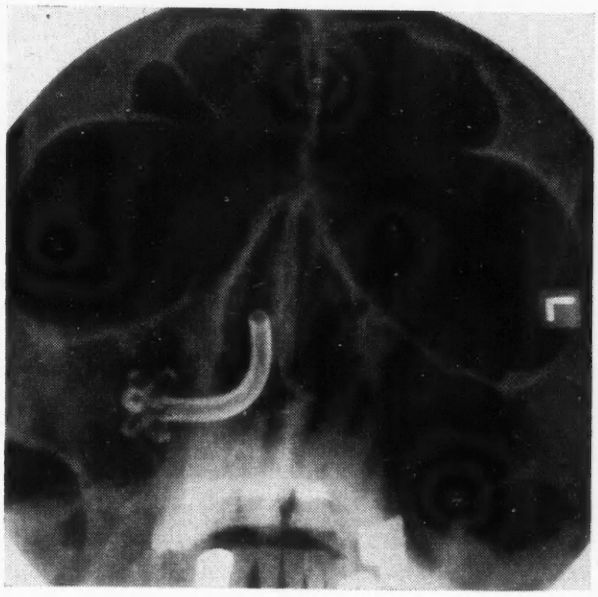

Fig. 2.—Subacute infection in the right antrum, with the catheter in place.
These instruments are manufactured by Storz Instrument Co., 4570 Audubon Ave., St. Louis, 10, Mo., U.S.A.

as this can be left in place for three or four weeks without causing any discomfort.

When the frontal sinus is involved almost invariably the corresponding antrum is also infected. Shrinking of the middle meatus to get dependent drainage and appropriate treatment to the antrum usually clears up the condition. Probing the frontal sinus in the presence of an acute infection is not without danger. In the subacute stage irrigation may be attempted but if the ostium is obstructed removal of a little redundant tissue in the middle meatus will often open up the fronto-ethmoid region.

As the ethmoid cells are variable in number and cannot be irrigated displacement treatments are of value, particularly in the subacute stage. This form of treatment was first described by Proetz[2] in 1926 and is especially useful in low grade infections of the ethmoid and sphenoid sinuses. By this means thick, sticky secretion is removed allowing the cilia to function normally. Usually a mild solution of ephedrine sulphate ½ or 1% in saline is sufficient or ¼ or 1% neosynephrine.

Many eminent rhinologists use the antibiotics locally in the hope of clearing up infection in the sinuses. Penicillin in saline has been given by displacement and good results obtained. Others claim that streptomycin adds a synergistic action to the penicillin and is more effective when a mixed type of infection is present. It is true that 5,000 units of penicillin per 1 c.c. of saline does not injure the cilia or interfere with ciliary action[3] and that penicillin being alkaline is not neutralized by the acid streptomycin. On the other hand, once the organisms reach the submucosa and the glands, it is difficult to see how the antibiotics are effective when used intranasally.

Theoretically, at least, once the irritant is removed by a mild shrinking saline solution, the inflammation tends to subside. Occasionally subacute infections with residual discharge in the sphenoid fail to respond to displacement treatments of ephedrine in saline. Catheterization then is often necessary to clear up the infection. Various cannulas have been devised for this procedure. As the approach is entirely nasal it is important for anyone attempting to probe this sinus to be familiar with the landmarks. Usually a few irrigations are sufficient and once ventilation is established the lining membrane tends to return to normal.

SUMMARY

An attempt has been made to describe our present day treatment of acute and subacute sinusitis. With the appearance of newer antibiotics without disagreeable side effects perhaps our treatment in these conditions will be more conservative in the future.

REFERENCES

1. PROETZ, A. W.: Applied Physiology of the Nose, Annals Publishing Company, St. Louis, 1941.
2. *Idem*: Displacement, Annals Publishing Company, 1926.
3. TREMBLE, G. E. AND SMITH, F.: *Canad. M. A. J.*, 53: 564, 1945.

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STUDIES ON THE FUNGISTATIC POWERS OF A NEW BENZOTHIAZOL AND AN ANTIHISTAMINIC COMPOUND*

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RECENT REPORTS on new fungistatic agents[1, 5, 6, 7] instigated comparative investigations *in vitro* of two compounds. Firstly, the antihistaminic drug, thephorin (2 methyl-9-phenyl-2, 3, 4, 9-tetrahydro-1 pyridindene hydrogen tartrate) and secondly, asterol dihydrochloride (2 dimethylamino-6-(betadiethylaminoethoxy-benzothiazole) both supplied by Hoffmann La Roche Inc.

SENSITIVITY AND SPECTRUM OF EFFECTIVENESS OF THEPHORIN AND ASTEROL DIHYDROCHLORIDE

In mycophil broth (Baltimore Biological Laboratory) final concentrations of 0.03, 0.07, 0.15, 0.3125, 0.625, 1.25, 2.5 and 5 mgm./ml. of thephorin and asterol dihydrochloride were prepared and the tests were carried out as described by Carson and Campbell.[1] The results of these experiments are shown in Tables I and II.

TABLE I.

INHIBITORY EFFECT IN VITRO OF THEPHORIN ON RECENTLY ISOLATED STRAINS OF PATHOGENIC FUNGI

Organism	*No. strains tested*	*Complete* inhibition*	*Partial† inhibition*
Candida albicans	3	5.00	5.00
Trichophyton			
mentagrophytes	2	0.3125	0.15
tonsurans	3	0.625	0.3125
violaceum	2	0.15	0.7
rubrum	1	0.625	0.3125
rosaceum	1	0.3125	0.15
concentricum	1	0.15	0.07
Microsporum			
audouini	1	0.3125	0.15
canis	1	0.3135	0.15
fulvum	1	0.625	0.3125
Epidermophyton			
floccosum	2	0.3125	0.15

In comparing the two substances on the basis of the common organisms tested, asterol dihydrochloride showed complete inhibitory action against *Candida albicans,* whereas concentrations of 5 mgm./ml. of thephorin showed only partial inhibition. A concentration of 0.315 mgm./ml. of asterol dihydrochloride proved to be effective against all dermatophytes tested, while with thephorin the effective inhibitory concentrations varied with the species tested.

TABLE II.

INHIBITORY EFFECT OF ASTEROL DIHYDROCHLORIDE ON RECENTLY ISOLATED STRAINS OF PATHOGENIC FUNGI

Organism	*No. strains tested*	*Complete* inhibition*	*Partial† inhibition*
Candida albicans	2	5.00	2.5
Trichophyton			
mentagrophytes	1	0.3125	0.15
rubrum	1	0.3125	0.15
Microsporum			
audouini	2	0.3125	0.15
fulvum	1	0.3125	0.15
Epidermophyton			
floccosum	1	0.3125	0.15

*Complete inhibition as confirmed by subculture of 0.01 c.c. of drug broth concentration to Sabouraud glucose agar and incubated at 28°c. for 10 days.

†Partial inhibition—Mgm./ml. of drug concentration that restricted growth to approximately 30 to 40% of growth in controls containing no drugs.

THE FUNGISTATIC EFFECT OF THEPHORIN AND ASTROL DIHYDROCHLORIDE AGAINST TRICHOPHYTON MENTAGROPHYTES

The penicylinder method of assay[3] was employed using Sabouraud glucose agar containing horse serum in a final concentration of 10%. The media was adjusted to pH 7.0. Petri dishes containing the serum-added glucose agar in 20 ml. amounts were prepared and allowed to solidify. Aqueous solutions of the compounds were added to the penicylinders on plates streaked with a ten day old culture of *Trichophyton mentagrophytes* and results were determined after ten days' incubation at 28° C. (see Table III).

TABLE III.

PENICYLINDER ASSAY OF ASTEROL DIHYDROCHLORIDE AND THEPHORIN USING TRICHOPHYTON MENTAGROPHYTES

	Area of Inhibition in cm.				
Concentrations mgm./ml	10.0	5.0	1.0	0.5	0.25
Asterol dihydrochloride	5.5*	5.5*	5.0	4.5	3.5
Thephorin	5.5	5.0	4.0	3.5	2.0

*5.5 cm. in diameter represent zones of complete inhibition (clearing to edge of Petri dish). Other figures denote complete inhibition for the area measured.

It was noted that asterol dihydrochloride showed complete clearing of the plate 5.5 cm., at concentrations of both 10 and 5 mgm./ml.,

*From the Department of Bacteriology and Immunology, McGill University, Montreal.
(This investigation was aided by a contribution from Hoffmann La Roche Inc.)

whereas thephorin acted to the same degree only at a concentration of 10 mgm./ml.

THE FUNGISTATIC EFFECT OF ASTEROL DIHYDROCHLORIDE AND THEPHORIN AGAINST MICROSPORUM AUDOUINI

While these studies were being carried out, asterol dihydrochloride was used for treatment of an epidemic of ringworm of the scalp of children in Sault Ste. Marie, Ontario, caused by *Microsporum audouini*. Asterol was supplied for treatment as a 2% tincture in 70% alcohol, and as a 2% ointment in carbowax 1,500. Infected hairs detected by a Wood's light, sent from the endemic area, were cultured on Sabouraud glucose agar. Of the total number of 58 specimens received for diagnosis, 54 gave cultures of *Microsporum audouini*. Upon receiving treatment for a period of six to seven weeks, 54 specimens were sent for diagnosis. Forty-six received treatment with asterol dihydrochloride, the remaining eight cases received another treatment. All specimens received gave cultures of *Microsporum audouini*. Further *in vitro* tests using asterol dihydrochloride and thephorin were carried out with these cultures of *Microsporum audouini* and determinations were made of the critical fungistatic dilutions by the agar plate method[4] using both asterol and thephorin.

The efficacy of many reportedly inhibitory agents has been shown to be greatly reduced by the presence of serum in the test medium.[3, 4] Using the agar plate method with *Microsporum audouini* as the test organism in the absence of serum protein, the critical fungistatic dilution of asterol dihydrochloride was found to be 1:128,000. However, in the presence of 10% serum added to the medium the critical fungistatic dilution was 1:16,000. The highest dilution of the test material which completely inhibited the growth of the organism was regarded as the critical fungistatic dilution.

Other authors[5] studying the properties of asterol dihydrochloride, in failing to use serum, have obtained higher critical fungistatic dilutions, and therefore these results cannot be strictly compared with their results.

In all tests and results to follow a 10% serum concentration in the form of horse serum was employed.

Both thephorin and asterol dihydrochloride were used in the agar plate determinations and they were diluted in 70% alcohol. The results of these experiments are shown in Table IV.

TABLE IV.

CRITICAL FUNGISTATIC DILUTIONS OF ASTEROL DIHYDROCHLORIDE AND THEPHORIN ON RECENTLY ISOLATED STRAINS OF MICROSPORUM AUDOUINI

Strain No.	*Thephorin*	*Asterol dihydrochloride*
I	1:8,000	1:16,000
III	1:8,000	1:16,000
IV	1:8,000	1:16,000
V	1:4,000	1: 8,000
VI	1:8,000	1:16,000
VII	1:8,000	1:16,000
VIII*	1:8,000	1: 8,000
IX	1:8,000	1:16,000
X*	1:4,000	1: 8,000
XI*	1:8,000	1: 8,000
XII	1:2,000	1:16,000
XIII*	1:4,000	1: 8,000
XIV	1:4,000	1:16,000
XV	1:4,000	1: 8,000
XVI	1:8,000	1:16,000
XVII	1:8,000	1:16,000

*Denote strains isolated from children who had received asterol dihydrochloride treatment for two days only.

Controls with 70% alcohol, using 0.1 c.c. per plate exerted no fungistatic effect upon the test organisms.

This table shows that the range of complete inhibition of growth by thephorin lies between a dilution of 1:2,000 to 1:8,000, whereas with asterol dihydrochloride the range lies between a dilution of 1:8,000 to 1:16,000. The possibility of resistance to asterol dihydrochloride by the strains of *Microsporum audouini* isolated from the children who received asterol dihydrochloride for only two days is noted in the lowering of the critical fungistatic dilution values and this is dealt with in the investigations to follow.

ACQUIRED RESISTANCE OF STRAINS OF MICROSPORUM AUDOUINI TO ASTEROL DIHYDROCHLORIDE

Seven representative cases of ringworm of the scalp caused by *Microsporum audouini* were selected for the study of acquired resistance and tests employing the agar plate critical fungistatic dilution method and the mycophil broth sensitivity test were carried out (see Tables V and VI).

It was noted that the sensitivity of *Microsporum audouini* isolated from the same case showed a steadily increasing resistance to the drug used in the course of treatment. It required an increase in concentration from 0.15 (strain VII) to 5.00 mgm./ml. (strain K), when the patient had been on treatment with asterol

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TABLE V.

MYCOPHIL BROTH SENSITIVITY DETERMINATION ON STRAINS OF MICROSPORUM AUDOUINI SHOWING DEVELOPMENT OF ACQUIRED RESISTANCE TO ASTEROL DIHYDROCHLORIDE

Strain No.	*Length of treatment*	*Complete inhibition*	*Partial inhibition*
VII*	No treatment	0.15	0.07
X*	2 days	1.25	0.625
K*	6 weeks	5.00	2.5
C	6½ weeks	5.00	5.00
H	7 weeks	5.00	6.00

*Denote strains of *Microsporum audouini* isolated from the same patient. Figures represent the drug concentration in mgm./ml.

dihydrochloride for only six weeks. As treatment proceeded strains of *Microsporum audouini* were isolated showing high degree of *in vitro* resistance to asterol dihydrochloride.

TABLE VI.

DEVELOPMENT OF ACQUIRED ASSISTANCE BY MICROSPORUM AUDOUINI TO ASTEROL DIHYDROCHLORIDE USING THE CRITICAL FUNGISTATIC DILUTION AGAR PLATE METHOD

Strain No.	*Length of treatment with asterol dihydrochloride*	*Critical fungistatic dilution*
13	No treatment	1:8,000
VII*	No treatment	1:16,000
X*	2 days	1:8,000
K*	6 weeks	1:2,000
D	6½ weeks + other treatments	1:2,000
H	6½ weeks (spreading infection)	1:1,600
(13)	6 weeks	1:2,000
(15)	7½ weeks	1:2,000

*Denotes strains of *Microsporum audouini* isolated from the same patient.

From these results, it was noted that within a period of six weeks, the critical fungistatic dilution dropped from 1:16,000 to 1:2,000 indicating the increasing resistance of *Microsporum audouini* to asterol dihydrochloride as treatment proceeded.

Microscopic examinations of agar plates at dilutions of 1:3,200 and 1:4,000 showed an increase in the number of chlamydospores from the number present in an untreated strain of *Microsporum audouini*. As the dilutions increased, the effect of the drug decreased and the colonies of *Microsporum audouini* showed the more typical mycelial structure.

SUMMARY

In vitro studies have been carried out on asterol dihydrochloride (2-dimethylamino-6-(beta diethylaminothoxy-benzothiazole) and thephorin (2-methyl-9-phenyl-2, 3, 4, 9-tetrahydro-1-pyridindene hydrogen tartrate) using three methods to determine their fungistatic properties: mycophil broth sensitivity test; the agar plate technique to establish the critical fungistatic dilution; and the penicylinder assay method.

Results obtained from these tests suggest that both asterol dihydrochloride and thephorin possess *in vitro* fungistatic properties for pathogenic fungi. Using the mycophil broth sensitivity test, asterol dihydrochloride in a concentration of 0.3125 mgm./ml. inhibited the growth of the dermatophytes, while the effective inhibitory concentration of thephorin varied with the species under study. Fungistatic properties of both compounds were shown with the penicylinder assay technique using *Trichophyton mentagrophytes*.

With the agar plate method, the development of resistance to asterol dihydrochloride was demonstrated in cultures of *Microsporum audouini* isolated from cases of ringworm of the scalp, when treatment with asterol dihydrochloride had been administered for six to seven weeks.

REFERENCES

1. CARSON, L. E. AND CAMPBELL, C. C.: *Science*, **111**: 689, 1950.
2. CAMPELL, C. C. AND SASLOW, S.: *Proc. Soc. Exper. Biol. & Med.*, **70**: 562, 1949.
3. HILLEGAS, A. B. AND CAMP, E.: *J. Invest. Dermat.*, **6**: 217, 1945.
4. OSTER, K. A. AND GOLDEN, M. J.: *Am. J. Pharm.*, **121**: 375, 1949.
5. GRUNBERG, G., SOO-HOO, G., TITSWORTH, E., RESSETAR, D. AND SCHNITZER, R. J.: *Bull. New York Acad. Med.*, ser. 2, **13**: 22, 1950.
6. REISS, F.: *Bull. New York Acad. Med.*, ser. 2, **13**: 28, 1950.
7. STRITZLER, C., FISHMAN, I. M. AND LAURENS, S.: *Bull. New York Acad. Med.*, ser. 2, **13**: 31, 1950.

In selecting an operation for glaucoma, the surgeon should be entirely familiar with current knowledge regarding fields, but as no two cases are alike he has great latitude in choosing his operation. Every glaucoma patient becomes a grave responsibility, and the surgeon must be conscious of this and plan his management carefully. With the tension and the fields as indices to the choice of operation and by adhering to sound surgical principles based on a thorough knowledge of the mechanics of the disease, he is on the only ground he may occupy in the treatment of this most aberrant of all surgical eye diseases.—Atkinson, J.: Internat. Coll. Surgeons, July, 1951.

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CASE REPORTS

ACUTE PORPHYRIA*

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PORPHYRIA IS A RARE DISEASE which is characterized by the appearance of abnormal porphyrins, principally uroporphyrin, in the urine. It was called one of the "inborn errors of metabolism" by Garrod. The etiology of the disease and the nature of the disordered metabolism remain quite obscure. In 1947 Linder[1] reported two patients with acute porphyria in whom the mineral metabolism suggested a state of relative adrenal failure. A similar observation was made by Abrahams *et al.*[2] These reports and the obscure nature of the disorder prompted the authors to study the effect of cortisone on a patient with porphyria in this hospital. It was hoped that such a study might throw further light on the metabolic errors involved in this disease.

Porphyrias can be divided into two main types, a congenital type and an acute type, and a rarer mixed type.[3] The congenital type occurs early in life, is more common in males and is characterized principally by photosensitive and cutaneous manifestations and red discoloration of the teeth. The acute type is more common than the congenital type. It occurs most frequently in females, in early adult life, is frequently intermittent and the symptoms involve primarily the gastro-intestinal tract and nervous system. The rarer mixed type exhibits the principal features of both the more common types. Some authors refer to this as chronic porphyria.

There are differences between these types with respect to the porphyrin excreted in the urine. In the congenital type the urine is usually continuously red in colour and large amounts of uroporphyrin Type I isomer are excreted. In the acute type the urine may be free of abnormal pigment during the latent phases of the disease. The uroporphyrin in this type is excreted largely in the form of a zinc complex. In the acute type there is also a colourless compound present in the urine called porphobilinogen. This relationship of porphobilinogen to the porphyrin is not clearly understood. On standing porphobilinogen forms porphobilin, a red brown non-porphyrin pigment, which accounts for much of the dark colour in the urine in acute porphyria. Schwartz and Watson have described a simple test for the detection of porphobilinogen in the urine based on the property of this compound to react with Ehrlich's aldehyde reagent resulting in the production of a pink colour. This porphobilinogen-aldehyde compound is insoluble in chloroform which distinguishes it from the pink urobilinogen-aldehyde compound which is soluble in chloroform.

Acute porphyria may present clinically in a variety of ways. The nervous manifestations may be confused with poliomyelitis, encephalitis, Landry's paralysis, lead poisoning, progressive muscular atrophy or hysteria. The predominant gastro-intestinal symptom is pain. It is variable in type and location. It may be confused with bowel obstruction, renal colic or acute appendicitis. Constipation of a severe degree is common. Physical signs are usually absent. The urine may be normal in colour when it is passed. The employment of Schwartz and Watson's test for porphobilinogen provides a simple means for establishing the diagnosis.

The case to be described is of the acute variety.

CASE REPORT

A 34 year old married farmer was referred by Dr. W. A. Henry of Lacombe, Alberta, to the University Hospital on November 5, 1950 with a diagnosis of acute porphyria. He had complained of chills, severe crampy lower abdominal pain and the passage of dark urine for a period of two weeks. Additional symptoms were intractable constipation and difficulty in voiding. No drugs or medicine of any kind had been taken prior to the onset of symptoms.

Examinations revealed a very ill young man, curled up in bed with his knees on his chest and perspiring profusely. The ocular fundi showed spasm of the arterioles. The pulse was 80, regular, and the systolic blood pressure was 150 mm. of mercury and the diastolic 95 mm. The abdomen was excruciatingly tender especially in the lower region and the cremasteric muscles were in spasm, drawing the testicles near the inguinal canals. Mentally the patient was normal. Porphobilinogen was identified in the urine by Schwartz-Watson's test, thus confirming the diagnosis of acute idiopathic porphyria. Large doses of meperidine hydrochloride (demerol) were needed for the control of pain.

Immediately prior to the institution of cortisone therapy on November 20, 1950, the urinary 17 ketosteroid excretion was found to be 4.2 mgm. for 24 hours. On December 3, he began to feel much better, became ambulant and suffered relatively little pain which was easily controlled with codeine. He began to eat freely and enemata were no longer necessary to relieve the constipation. The abdominal and testicular tenderness disappeared, he ceased to sweat excessively and was cheerful and talked of going home. Roentgen examination of the gastro-intestinal tract was carried out between December 18 and 20, to rule out any organic disease. These investigations were essentially negative although

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the passage of barium through the stomach was somewhat slow.

On December 23, during cortisone therapy, the abdominal pains, vomiting, and the obstinate constipation recurred. Subsequently he vomited frequently throughout the day and the abdominal pain was of such severity as to require the use of large doses of sedatives, methadon hydrochloride 15 mgm. every 2 hours; meperidine hydrochloride 100 mgm. every 2 hours and methyl dihydromorphine (metapon), 8 mgm. every 8 hours. Even with this therapy the patient was not free of pain.

On January 21, 1951 neurological signs appeared. He became very unsteady, unable to hold a glass of water without splashing its contents and a weakness appeared which progressed rapidly to the point of complete flaccidity and paralysis of all leg and arm muscles. All tendon reflexes were absent but sensations remained intact. During the last four weeks of his illness he was unable to open his jaws completely. No explanation was found for this phenomenon.

Two days following the cessation of cortisone therapy on January 6, 1951 a second determination of urinary 17 ketosteroid excretion was 5.2 mgm. for 24 hours. A total of 5.75 gm. of cortisone had been given. Blood electrolytes, including estimation of potassium, sodium, chlorides and calcium at various times were always reported to be within normal limits. Periodic daily quantitative estimation of the urinary porphyrin excretion was carried out by the Department of Biochemistry at the University of Alberta (See Chart No. 1). This ranged

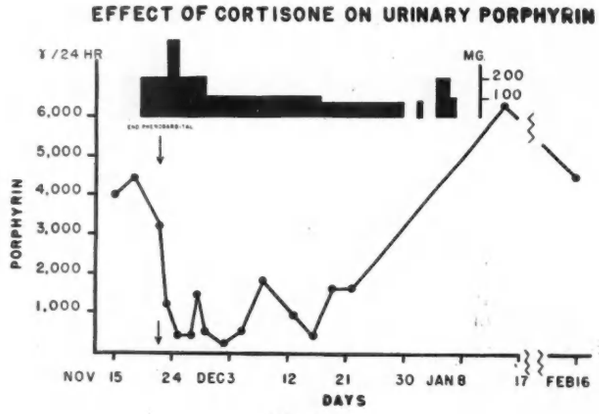

Chart 1

from a maximum of 4,400 μg. per day prior to treatment to between 227 to 1,847 μg. per day during the period of cortisone therapy. Following exacerbation of symptoms in the latter part of December 1950, his porphyrin excretion increased to approximately the 3,000 μg. level and exceeded 6,000 per 24 hours on January 17. The hæmoglobin did not fall appreciably until the terminal stage of the illness.

Serial electrocardiographic findings were normal throughout and showed no evidence of potassium deficiency.

Various medications were tried to alleviate the symptoms and to treat the underlying disease. Noteworthy amongst these was pantothenic acid which was given daily with other vitamins of the B complex* by intramuscular injection. Phenobarbital, gr. 1½, t.i.d. had been inadvertently ordered on admission and was given for the initial two weeks. Methyl cellulose was tried unsuccessfully in an attempt to alleviate the constipation. Prostigmine was administered with the hope that his neurological symptoms might improve. Since porphyrin is excreted as a zinc complex this element was administered by mouth as zinc sulphate to obviate the possibility of any deficiency of that metal late in the disease. All such medications proved ineffectual.

There was a marked loss of weight from 160 lb. on admission to 110 lb. on January 10, 1951, after which time weighing was impossible because of the enfeebled condition of the patient. During the terminal three weeks of the illness, swallowing was virtually impossible because of paresis of the muscles of deglutition. He spoke only in a hoarse whisper and was maintained on approximately 2,000 c.c. of intravenous fluids daily.

The patient died 104 days following admission to the hospital. An autopsy was performed by Dr. D. R. Waugh, of the Department of Pathology, whose findings are summarized as follows.

Autopsy performed 6 hours post-mortem revealed the changes of bronchopneumonia of the left lung, left hydrothorax (400 c.c.), slight hydropericardium, and ascites (500 c.c.). The fluid in each of these accumulations was clear, amber and watery. The heart was small (250 gm.) but not otherwise abnormal. The most striking gross change was a uniform bright blue-gray discoloration of the liver and spleen. This change was also present but less marked in the kidneys and heart muscle. This bluish discoloration deepened to purple, almost black, within 30 minutes of exposure to air. The unexposed portions of the organs changed colour much more slowly.

On microscopic examination changes of chronic passive hyperæmia were seen in lungs, liver and spleen. Healed mediastinal tuberculous lymphadenitis was present. Unusual accumulations of bile pigment in liver cells suggested biliary stasis, although no evidence of biliary obstruction was demonstrated. Disintegration of myelin sheaths of lumbar sympathetic nerves apparently represented non-specific degenerative changes. Nerve cells themselves were unaltered. Sections of brain, adrenals, pancreas, thyroid, pituitary, testis, prostate, bone marrow and intestinal tract showed no abnormality. The immediate cause of death was considered to be bronchopneumonia.

DISCUSSION

The porphyrin excretion in this case began to fall immediately the cortisone was given and reached a minimum, but not normal level after five days of treatment. The excretion remained greatly reduced for over a month and two determinations of urinary porphyrin done after the cortisone was discontinued showed that the excretion had returned to the initial high level. Early in the period of cortisone therapy the patient showed some clinical improvement with less painful abdominal cramps but soon his condition deteriorated and he developed widespread involvement of the nervous system with paralysis. It would appear that although the porphyrin excretion was reduced the disease itself was not greatly altered.

Barbiturates have been described as precipitating attacks of porphyria. Unfortunately this man had been given phenobarbital, and was receiving this drug when treatment with cortisone was commenced. The phenobarbital was discontinued four days after the first dose of cortisone and its withdrawal coincided with the initial fall in porphyrin excretion. The significance of these changes in porphyrin excretion during cortisone therapy must be qualified to

*Given as B-plex (Wyeth).

some degree in view of the fact that barbiturates have been incriminated as precipitating agents in this disease. The patient gave no history of having taken any of these drugs immediately prior to the onset of symptoms and presumably therefore, they were not the precipitating factor in this case. A spontaneous remission coincidental with the institution of cortisone therapy cannot be excluded as the cause of the marked change in porphyrin excretion, although this is unlikely.

We are unable to offer any explanation as to the possible mode of action of cortisone in apparently bringing about a reduction in urinary porphyrin excretion in this case. Oltman and Friedman[4] recently reported no change in porphyrin excretion following the administration of ACTH to a patient with acute porphyria.

SUMMARY

A case of acute porphyria treated with cortisone is presented. During the period of cortisone therapy the urinary porphyrin excretion was greatly reduced but the therapy failed to influence the fatal course of the disease.

The authors wish to acknowledge the valuable assistance given them by Dr. Jules Tuba, of the Department of Biochemistry, of the University of Alberta, who carried out the porphyrin determinations, and the clinical assistance and advice of Dr. F. J. Elliott.

REFERENCES

1. LINDER, G. C.: *Lancet*, **2**: 649, 1947.
2. ABRAHAMS, A., DAVEY, C. J. AND MACLAGAN, N. F.: *Brit. M. J.*, **2**: 327, 1947.
3. WATSON, C. J.: *Lancet*, **1**: 539, 1951.
4. OLTMAN, J. E. AND FRIEDMAN, S.: *New England J. Med.*, **244**: 173, 1951.

NEUROMYELITIS OPTICA

(*Devic's Disease*)

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THE SIMILARITY and somewhat restricted histopathological responses of nervous tissue to infective and toxic processes makes the differentiation of demyelinizing diseases of the nervous system most difficult. Symptom-complexes, depending on which areas of brain and cord are involved, together with the rate of progression of the disease process, more often delineate the clinical entity than the pathological findings.

In the differential diagnosis of central nervous system disease associated with destruction of myelin, disseminated sclerosis, Schilder's disease, and diffuse encephalomyelitis are the most important. Whether the disease to be described is another entity in addition to these or a manifestation of encephalomyelitis is not known.

The unanswered questions are—are these the same disease with variation in onset, localization, and intensity; or separate clinical entities? Is the etiology the same?

In 1870 C. T. Allbutt first recorded a case of acute myelitis associated with eye-symptoms. Following this report in *The Lancet* several other observers recorded similar cases. In 1894 Devic fully described the syndrome which he called "Neuromyelitis optique aigue" and subsequently his name was attached to the syndrome.

Clinical features.—The onset of an acute neurological disorder characterized by paraplegia with partial or complete sensory loss and paralysis of the sphincters suggests a transverse or ascending type of myelitis.

When this acute condition is associated with visual disturbance or loss, the following entities must be considered, namely, acute encephalomyelitis, acute disseminated sclerosis. Schilder's disease and neuro-myelitis optica. The separation of these diseases may be difficult at the onset.

The age incidence of multiple sclerosis seldom occurring before 12 years and after age 55, may be of value, as no age limits are known for neuro-myelitis optica, which can occur in very early childhood or old age. The presence of cerebellar involvement, nystagmus, and the rarity of bilateral ocular involvement suggest disseminated sclerosis.

The bizarre and varying visual fields are more diagnostic of Schilder's disease, which is usually associated with a spastic instead of a flaccid paralysis and rarely involves the cord pathologically. In neuro-myelitis optica the cord is practically always involved. Most difficult to separate is diffuse encephalo-myelitis, when there is absence of an acute infection at the beginning of the disease, and at present neuro-myelitis optica may be an identical disease.

Although most reported cases indicate the visual loss following the onset of paraplegia, there are recorded cases in which it has preceded or occurred simultaneously with it. The eye-signs are mostly loss of visual acuity field defects or total blindness. There are seldom signs of internal or external ophthalmoplegias. The

ocular fundi vary from normal appearing discs to pallor of the entire nerve-head. Mild papillo-œdema often erroneously suggests intra-cranial tumour. The cerebrospinal fluid findings are not diagnostic. The dynamics are usually normal. There is normal or only very slight increase in protein and very little cellular response except in very acute phases. The negative spinal fluid Wassermann rules out syphilis.

The course of the disease is variable and unpredictable with recessive tendency in mild cases, and usually subsequent sequelæ, or progression to bulbar paralysis and respiratory failure. For this reason the prognosis must be guarded as the disease carries a formidable mortality rate of 50%.

The following case report fulfills the criteria described by Devic and is presented as a case of neuro-myelitis optica.

CASE REPORT

Mrs. E.G., a 50 year old white female, was admitted to hospital on January 28, 1948 for investigation. She was apparently well until January 19, 1948 when she first noticed epigastric tenderness. Two days later she experienced headache and pain in the right shoulder. On January 22, she complained of backache and the next evening noticed increasing difficulty in maintaining her balance on walking. She also noticed a beginning difficulty in voiding. The next day a doctor was called to catheterize her because of her inability to empty the bladder. On January 25, sensory loss began to appear over both lower limbs and by January 27, she felt inability to feel or move both lower extremities and a band sensation across her lower abdomen. She had no bowel movement for at least 5 days and required an enema. There was no disturbance of vision and no history of recent trauma.

Her past history was non-contributory except that she was once given dilute hydrochloric acid for achlorhydria. She had an early menopause at age 33 and had no children.

The clinical examination showed a flaccid paralysis of both lower extremities with complete anæsthesia. The tendon reflexes were absent and there was a loss of vibration sense. There was no plantar response. The tendon reflexes were present in both arms. The abdomen was very distended with loss of abdominal reflexes and there was loss of sensation to the level of the xiphoid process.

The remainder of the examination showed the pupils to be equal and react to light and convergence. The ocular fundi were negative. The lung fields were clear, with unrestricted and full chest movement. The heart was normal in size, regular in rate and rhythm with blood pressure 140/105.

X-ray of the chest was negative. The A-P and lateral exposures of the dorsal and lumbar spine showed slight osteo-arthritic lipping in the region of thoracic 7, 8 and 9. There was some diffuse decalcification of bone, but no evidence of pathological fracture.

A spinal tap done on the day of admission showed the spinal fluid to be under normal pressure, normal spinal fluid dynamics. The spinal fluid Wassermann was negative. There were no cells, 24 mgm. of protein and normal reducing bodies. The red blood count was 4,470,000, Hb. 13.51 gm., the white blood count 7,000, with normal differentiation. The urinalysis was negative, and there was no evidence of porphyrinuria.

The temperature was 101° F. This continued during her entire hospital period.

A diagnosis of acute ascending myelitis was made and treatment of an expectant nature carried out. She was given large doses of thiamine chloride by mouth and parenterally. An indwelling catheter with tidal drainage was instituted, and prophylactic therapy for the prevention of decubitus ulcers. The patient was moved frequently from side to side. In spite of therapy she developed an ascending pyelo-nephritis and by February 15, showed innumerable pus cells in the catheterized urine. She was put on streptomycin and sulfanamides and by February 22, the urine was clear. The fever still persisted and the hæmoglobin dropped to 8.93 gm. (57%), for which she was given a 500 c.c. transfusion of blood. About February 22, she began noticing some weakness in the hands and arms. The clinical examination showed definite muscle weakness and diminishing tendon reflexes in both arms, but most prominent in the left.

On February 29, a repeat spinal fluid showed an increase of protein to 64 mgm. %. There were no cells. At this stage her disease appeared to remain stationary and on March 5 she had a normal bowel movement. On March 18, physiotherapy to the lower extremities and ultra-violet light to the entire body was begun. By April 3, she was allowed to sit up in a chair for one-half hour morning and afternoon. The bladder paralysis persisted and she had retention with overflow. She had involuntary bowel movements at times. Periodic red blood counts showed values that fell to 3,000,000 cells with 60% hæmoglobin, and serial urinalysis varied from many pus cells to none

For the next three months until the time of her discharge, the condition did not progress. There were days when slight leg movement could be made out. There were times when she had some bladder control, followed by periods of incontinence. The bowels moved with enemata or glycerine suppositories, and were often involuntary.

She was discharged on July 20, as a chronic invalid but with a normal blood count and Hgb of 15.96 gm. She periodically had some control over the bladder and bowels. The reflexes were still absent and sensory and motor loss over the lower extremities reaching to the level of the xiphoid remained constant.

Second admission.—The patient was re-admitted April 15, 1949. During the interval she had been a patient in two other hospitals. On this admission the physical examination showed complete loss of voluntary motion in both lower extremities, with anæsthesia and bladder and rectal incontinence. There was hypotonicity, and a positive Babinski sign on the right with ankle clonus. There was definite weakness in the left arm. There was vertical and horizontal nystagmus in both eyes. She had great diminution in the visual fields and could not discern objects more than 6 inches distance. Vision in the temporal fields was completely absent. The ocular fundi showed marked pallor of the discs indicative of early optic atrophy.

Laboratory investigation April 16, showed red cells 4,880,000, Hgb 12.8 gm., W.B.C. normal, urinalysis 30-40 pus cells per high power field. The urine showed numerous Gram-positive cocci, and coliform bacilli. The spinal fluid was under normal pressure, with no cells and protein slightly increased at 62 mgm. %. Blood urea was 40 mgm. %.

The subsequent course in hospital was progressively downhill with episodes of temperature and gross pyuria. She passed several bladder stones per urethram, these, on examination, were a mixed type of calcium and magnesium phosphates and oxalates. She was a difficult nursing problem, developing flexor contractions of hands and lower extremities, decupitus ulcers over both heels and sacrum. On August 27, she lapsed into coma and died on August 30, 1949.

AUTOPSY

The main pathological changes were as follows. There was an abscess filled with greenish foul-smelling fluid pus in the neighbourhood of the upper pole of the left

kidney. This abscess was partly enclosed by the kidney substance and partly by surrounding perinephric fat. It also appeared to be draining into the pelvis of the kidney but there was no real suppuration of the pelvis or of the kidney substance.

The brain (1,407 grams) was of normal size and on sectioning nothing unusual could be found by naked eye examination. The cord was grossly normal.

HISTOLOGY OF THE CORD AND BRAIN

The lumbar cord shows much demyelinization with little cellular reaction now visible. The affected areas are widespread and somewhat patchy in distribution but seem to be favouring the anterior part of the cord more than the posterior. A little perivascular cuffing with lymphocytes is present. There is little evidence of gliosis.

The appearances seen in the cervical portion of the cord are similar but here a cellular reaction is taking place and many histiocytes with foamy cytoplasm are visible. In the medullary region of the brain stem a similar process is present but this is more patchy and somewhat less diffuse than that seen in the spinal cord.

Many areas of the brain show patches of demyelinization. Some of these are at different stages. In the more recent ones there is a fairly marked cellular reaction and numerous phagocytes are seen and there is much perivascular cuffing. In the later ones little cellular reaction is visible and in one or two areas almost complete liquefaction of the brain substance appears to have occurred.

SUMMARY

The pathologist's report is that of a diffuse encephalo-myelitis of unknown etiology. Clinically the patient presented the picture of neuromyelitis optica. There is no "definitive" pathology, the diagnosis is made purely from the symptom-complex. The absence of gliosis in this case rules out multiple sclerosis pathologically but this disease cannot be separated from diffuse encephalo-myelitis *per se* except for the additional single clinical sign of visual disturbance. The probability that this is a distinctive and separate disease entity from diffuse encephalo-myelitis is doubtful.

BIBLIOGRAPHY

1. ALLBUTT, C. T.: *Lancet*, **1**: 76, 1870.
2. DEVIC, M. E.: *Cong. Franc de Medicine*, **1**: 434, 1894.
3. GOULDEN, C.: *Ophth. Society, United Kingdom*, **34**: 229, 1914.
4. MCKEE S. H. AND MCNAUGHTON, F. L.: *Am. J. Opth.*, **21**: 130, 1938.
5. WALSH, F. B.: *Bull. Johns Hopkins Hos.*, **56**: 183, 1935.
6. ARMENTROUT, C. H. AND PEASLEY, E. D.: *Ann. Int. Med.*, **32**: 129.

Aureomycin was successfully employed in the treatment of four cases of actinomycosis (three cervicofacial and one abdominal) without evidence of recurrence during post-therapeutic observation periods extending from twelve to seventeen months. *In vitro* sensitivity studies established a definite inhibitory action by aureomycin on *Actinomyces bovis*.—McVay, L. V., Guthrie, F. and Sprunt, D. H.: *New England J. Med.*, **245**: 91, 1951.

A CASE OF DOUBLE UTERUS

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F. H. MUNKLEY, B.A., M.D., *Saskatoon*

THE FOLLOWING CASE was felt to be of interest on account of its rarity.

Mrs. E. J. McK. was referred to us with symptoms of extensive menorrhagia accompanied by severe lower abdominal cramps. There had been a gradual onset two to three years ago with gradually increasing menorrhagia and low abdominal cramps. During the last six months her condition had become much worse. These bouts now lasted two to three weeks each month and she was either confined to bed, or, on two occasions, was in hospital due to pain and debility from blood loss. Her menses started at about 12 and there was nothing abnormal until seven years ago, when, during an apparently normal pregnancy, she had premature labour at seven months. The baby weighed 3 lb. 13 oz. and died in its eighth day. No more details could be found regarding this confinement. A general functional inquiry revealed nothing significant except an operation in 1948 for diseased gall bladder and appendix.

The general physical examination revealed some tenderness suprapubically and in both lower quadrants of the abdomen, but no masses were felt. An upper right rectus incision was noted. On inspection of the pelvis, anterior and posterior mid-line tags of mucosa were noted in the vagina and a septum running about an inch deep in the A.P. diameter was seen in the upper aspect of the vagina. Two distinct, separate cervices were noted, one on either side of the septum. On bimanual examination, two separate uterine bodies were vaguely felt. At this time her hæmoglobin was 64%, blood type A, Rh positive. This followed immediately after a transfusion she had had before referral. The urine showed no abnormalities.

Under anæsthetic, a probe was found to pass freely into the right uterine body and cervix but not past the internal cervical os on the left side. A connection between the two cavities was seen in the region of the internal cervical os. Definite sausage-shaped uteri were felt in the fornices in the form of a U. These were well anteverted and symmetrical.

At laparotomy, a U-shaped fusiform uterus was found with a flap of bladder triangularly shaped attached at the apex of the triangle over the base of the U of the body of the uterus and attached to the posterior aspect of it. A total hysterectomy was done. A plastic repair was felt inadvisable due to the possibility of a ruptured uterus with subsequent pregnancy because of the connection between the two cervical canals. No serious difficulty was incurred after the bladder flap was freed. A rather extensive incision was necessary in the vault of the vagina and the septum in the vagina was removed with the double cervix. A routine closure with oversewing of the fascia of the vaginal cuff was done. No complication occurred and she had an uneventful postoperative course.

Pathological report.—(Dr. D. F. Moore). Gross specimen consists of a double uterus with two exocervical openings. It weighs 104 grams and each corpus possesses one laterally-placed cornu with a tubal and round ligament stump. The left corpus measures 8 cm. from fundus to exocervix, 4 cm. in transverse diameter and 3 cm. in thickness. The right corpus measures 7.5 x 3.4 x 3 cm. Through separate cervical canals a probe can be passed readily to either fundus. The fused cervices measure 3 cm. in length x 5 cm. in transverse diameter x 2.5 cm. in thickness. A 1 cm. communication extends between two cervical canals and begins 1 cm. above the ora. Removal of the attachment of a vaginal septum reveals a raw strip, 0.4 cm. in greatest width, lying between two external ora. No sections are taken because the specimen is to be preserved for museum purposes.

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DISCUSSION

The case presented was one of a complete double uterus, the only connection being at the internal os of the cervices and this probably of traumatic origin. The condition is the consequence of an error of development of the Mullerian system particularly of the fusion of the lower parts to form one canal which later forms uterus, cervix and upper vagina. Bilateral or unilateral failure of development may occur. According to Wm. Hunter,[1] arrested development of one or both sides during the second month of interuterine life may cause the growth of a dichotomous, bicornuate or cordiform uterus with a double uterine cavity. In all cases the deformed uterus arises from two, or, in the case of the unicornuate uterus, one Mullerian duct, and each semi-uterus has only one associated uterine tube and ovary. Many cases are symptomless. The cervices do not show any abnormality from a normal cervix, and it is possible in an undiagnosed case to curette one uterine body and completely miss an incomplete abortion or carcinoma in an unexplored horn. The above author states that operation on a completely double uterus is not justifiable simply for correction of the uterine deformity, but is done to cure debility from pain and heavy blood loss. The discussed case is an example of the latter.

REFERENCE

1. HUNTER, W.: *J. Obst. & Gynæc., Brit. Emp.*, 57: 721, 1950.

A GIANT MELANOTIC MOLE

R. KERR DEWAR, M.D.(Man.), L.M.C.C., B.Sc.,(Edin.), F.R.F.P.S.(Glasg.), *Fort William, Ont.* and

CHARLES E. BAKER, M.D.(Man.), L.M.C.C., B.Sc.(Sask.), F.R.C.S.(Eng.), *Port Arthur, Ont.*

THIS CASE is reported because of the unusually extensive size and the character of the mole (Fig. 1). The patient was first seen by one of us (R.K.D.), when a year old, and after the mother had undressed the child the doctor stopped himself as he was about to request that she remove the child's coat—the "coat" being the mole in question. It extended at that time from within the hairline at the nape of the neck to the second lumbar spine inferiorly, and from the anterior axillary line on the one side right round to the corresponding line on the other. The mother explained that she had just had an extensive study done on the child at the Sick Children's Hospital at Toronto, and they had advised against operation as the child was not expected to grow up. The tumour was present at birth, and had not varied in relative size since then.

The patient had a younger sister with rather more moles than normal; they were of the same type.

From time to time the patient was seen by one of us, as family doctor, and palliative treatment prescribed. The main complaint was that of intolerable itching—the patient would almost at times seem to scratch herself to pieces. This pruritus was most marked superiorly, and along the edges of the tumour. The tumour mass itself was rolled into folds, and radiographically there was a faint calcium deposit throughout which showed on chest films as outlining the respective folds as they hung from the body. Luminal in small doses seemed to control the pruritus best, and was least habit-forming. The child was bright in school, and in due time it was decided

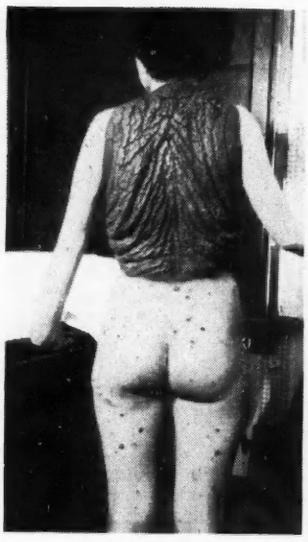

Fig. 1

Fig. 2

Fig. 1.—Patient, aged 15, showing giant mole extending across the back. Note the numerous moles throughout the skin areas apart from the main tumour mass itself. Photo before operation. **Fig. 2.**—Patient, aged 16, nine months after operation. Shows a distinct hair-line now, with the "V"-shaped depression at top of mole in midline where tumour tissue sloughed after operation.

to send her to high school. At the age of eleven the menstrual flow came on, and was regular. Secondary sex characteristics developed normally. The only symptom of note other than the itching was a sense of tiring after exertion. This was explained by the pulse-rate, which averaged around 120 beats per minute at rest, and more on exertion. Short and long-wave diathermy and ultra-violet light irradiation persistently administered at this time in accordance with the system outlined in a communication by one of the authors (R.K.D.),[2] brought the pulse-rate down considerably, and after a year's intermittent treatment it was around 105, with a feeling of subjective and objective improvement.

When 15, the patient was morose and introspective; she was not able to wear normal clothing like other girls, and had to have a silk scarf continually around her neck. The mother appealed for surgical aid, if possible.

Warren H. Cole[1] declares that such large moles never become malignant, though in our patient's case there were a very large number of smaller moles scattered throughout the body which, it was felt, would be a source of potential malignancy. Some of these can be seen in the photograph. Hæmorrhage and keloid were the two most feared complications, particularly keloid on the face, where some large, ugly-looking moles, subsequently removed, disfigured an otherwise good-looking physiognomy. Keloid was felt to be possible from its association with pigmentation, as with the negro race. It was felt, too, that by stages the whole massive mole could be removed, the first step being the cutting out of the individual small moles as they were present in cutaneous areas which would be turned in as flap grafts. (There would be no use transplanting moles, and care was taken to remove the entire mole in each case.) In all, about 150 moles were removed at one step, and only a few of the scars showed moderate keloid formation later, none of this, fortunately, being in visible parts.

The patient was fortified by blood transfusions and massive doses of antibiotics at the General Hospital, Port Arthur. The main operative procedure was planned three weeks later to remove the top part of the mole entirely to below the blouse neck line. For this purpose strap or epaulette flaps were raised from the front of the shoulders and turned back to cover the resultant defect. The removal of the tumour mass itself was accomplished very slowly, quarter-inch by quarter-inch, as the underlying bed was very vascular. Once the tumour mass had been turned down, however, it was cut off inferiorly with no bleeding of note. In all it was estimated that 120 square inches of mole were removed at this stage.

Postoperative progress was marked by a sudden high fever to 103° on the third day, (average temperature had been raised about half a degree over normal in this patient), and the cause was found to be a small area of gangrene in the tumour mass itself, right in the midline superiorly. This was fortunately limited in extent, however, and soon sloughed off. (It can be seen as healed in Fig. 2.) It was felt that strong retention sutures to keep flaps in place, too, were not justified on this account, and the flaps in healing gradually pulled away somewhat over a period of the next three weeks, so that Thiersch skin grafts had to be applied continually. Ultimately, however, healing was complete, and the patient was discharged in the fifth postoperative week.

It is now a year since operation, and continued treatment with physical therapy as outlined has further brought the patient's pulse down to around 90. Her strength is much improved, itching is much better, and she continues at high school. The mother in a recent letter states that the change is almost unbelievable. From a home-ridden patient her daughter now goes out with friends normally, and her mental outlook has radically changed for the better; she no longer lies and weeps by the hour, but enjoys life.

It is planned to continue the removal of the tumour mass in stages until it is completely gone; skin flaps have been outlined to allow this to be done—covering any remaining raw areas by Thiersch graft.

Pathological reports on the tumour material by Dr. A. E. Allin of the local provincial health laboratory show no evidence of malignancy.

REFERENCES

1. COLE, W. H.: Operative Technique, Specialty Surgery, p. 22, Appleton-Century-Crofts, Inc., New York, 1949.
2. DEWAR, R. K.: *Canad. M. A. J.*, **57**: 288, 1947.

Probably the most dramatically obvious of all the contrasts between medicine in 1868 and at the present day, is provided by a comparison between the resources available and used for medicinal treatment, then and now. It is a contrast between the empirical administration, then, of traditional remedies largely of no clearly recognizable activity and, in any event, with no expected result beyond the alleviation of certain symptoms; and, on the other hand, the present-day use, with confidence and precision, of remedies with clearly defined and measurable actions, many of them concerned with the direct removal of the causes of disease, and not merely with the assuagement of its symptoms.—*The Practitioner*, **167**: 314, 1951.

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SPECIAL ARTICLE

REPORT ON THE FORMATION OF THE CANADIAN PSYCHIATRIC ASSOCIATION

G. H. STEVENSON, M.D., F.R.S.C.,
London, Ont.

THE CANADIAN PSYCHIATRIC ASSOCIATION came into existence June 20, 1951, at its inaugural meeting held in Salon C of the Mount Royal Hotel in Montreal. This is therefore an historic date for the future records and archives of this first autonomous national association of Canadian psychiatrists.

Although this paper should be limited to the title assigned to it by the program committee, nevertheless it seems appropriate to review not only the steps leading to the formation of the Canadian Psychiatric Association, but also to mention briefly other organizations with which Canadian psychiatrists have been particularly identified since the beginning of psychiatric history in Canada.

No attempt will be made in this paper to discuss the development of psychiatric institutions in Canada as this subject was thoroughly covered in the 4 volume work published in 1918 entitled "Care of the Insane in the United States and Canada". However, the development of psychiatry as a specialty in Canada during the last 35 years could well form the subject of another paper and might be concerned with the improvement of psychiatric treatment procedures in our mental hospitals, the gradual emancipation of psychiatry from neurology, the development of the mental hygiene movement, the teaching of psychiatry in our medical schools at both the undergraduate and graduate levels, the introduction of psychiatry into the general hospitals and into private practice, the certification of specialists in psychiatry and the contribution of psychiatry in the two world wars.

The first organization in which Canadian psychiatrists held membership was the Association of Medical Superintendents of American Institutions for the Insane, which was the name by which the American Psychiatric Association was originally known. It was formed by thirteen American asylum administrators in Philadelphia in 1844. At its first meeting it agreed to admit Canadian asylum superintendents on equal terms and Dr. Walter Telfer, superintendent of the Lunatic Asylum at Toronto (as it was then called), attended the second meeting which was held in Washington, D.C. in 1846. Canadian psychiatrists have held membership continuously since that date. In 1892 its name was changed to the American Medico-psychological Association and in 1921 it became the American Psychiatric Association. In 1892, membership which formerly had been restricted to superintendents of mental institutions, was opened to all physicians specializing in mental disorders. Although Canadians constitute only a small percentage of its membership, they have always been treated with the greatest generosity by their American colleagues. Six Canadians have been honoured with the presidency of the American Psychiatric Association, many have served on its council and committees and several of the annual meetings have been held in Canadian cities. Formation of the Canadian Psychiatric Association will not deprive Canadians of membership in the American body, which in the future, as in the past, will continue to be the great meeting place for the psychiatric sciences and the exchange of psychiatric knowledge.

Although there has not previously been an autonomous body of Canadian psychiatrists, a section of psychiatry was established in the Canadian Medical Association in 1945. The first meeting of the section was held in 1946 and yearly meetings have been held since that date for the presentation of scientific papers. It should be noted, too, that as far back as 1929 a section of Mental Diseases was set up by the Canadian Medical Association with Dr. C. A. Porteous as chairman and Dr. E. C. Menzies as secretary, holding its first meeting in Montreal. The section held a meeting the following year in Winnipeg, in a conjoint meeting between the Canadian Medical Association and the British Medical Association. It appears that no further meetings were held until the present section on psychiatry was inaugurated in 1945.

One other national body deserves mention in this connection. The National Committee for Mental Hygiene (Canada) was established in 1918 by the late Dr. C. K. Clarke and Dr. C. M. Hincks. Dr. Clarke was probably the first Canadian psychiatrist to devote himself to preventive psychiatry. This body, which changed its name in 1950 to the Canadian Mental Health Association, has had relatively few psychiatrists actively participating in its work, but a great many Canadian psychiatrists have had liaison relationships with it of a very valuable sort, and its efforts have been outstanding for the improvement of mental hospitals, for the establishment of mental health clinics, for better mental health in all citizens through education, and for the encouragement of research in mental health and mental disease.

There are also several other psychiatric organizations of more circumscribed geographical areas. The Ontario Neuropsychiatric Association was founded in 1920, holding its first meeting at the Ontario Hospital, Kingston, with Dr. E. J. Ryan as president. It has no formal membership lists, and is sponsored by the Hospitals division of the Ontario Department of Health, chiefly for the education of the physicians in its own mental hospital service, but also for the benefit of other psychiatrists, neur-

ologists and physicians in other types of practice. Meetings are held in various parts of the province several times a year and papers delivered at its meetings are usually published in the Association's bulletin.

Psychiatrists in the Province of British Columbia join with their colleagues in the states of Oregon and Washington in the North Pacific Society of Neurology and Psychiatry, an affiliate society of the American Psychiatric Association. An annual meeting is held. Vancouver psychiatrists are also members in a section of neuropsychiatry of the Vancouver Medical Association, which section was established in 1945.

Although Saskatchewan does not have a definite psychiatric society, it has an approximation to it in what is called a Provincial Psychiatric Clinical Conference. This is a multi-professional organization, formed in 1949, for the improvement of mental health standards and facilities in various fields.

There is a psychiatric section of the Manitoba division of the Canadian Medical Association which was organized in 1947. Meetings are held four times a year. Likewise, in the Ontario Medical Association, a section on neurology and psychiatry was organized as recently as May 24, 1951, during the Ontario Medical Association meeting in Toronto.

It should also be noted that the Montreal Medico-chirurgical Society has had a Section of Psychiatry since 1933 (formed officially March 3, 1933). The Toronto Academy of Medicine likewise has had a section of Neurology and Psychiatry since 1933, the first meeting being held in January of that year.

Until comparatively recent decades the practice of psychiatry was confined to the mental hospitals. Even as recently as twenty-five years ago the only psychiatry in private practice was performed by neurologists, and the mental hygiene movement was barely started. Since then there has been a remarkable expansion of psychiatric fields of interest, such as the development of mental health clinics, the establishment of psychiatric services in general hospitals (still all too few), the extension of psychiatric services in the armed forces for the selection of recruits and the treatment of psychiatric disorders, the increase of personnel in the departments of psychiatry in our medical schools, the inclusion of the neuroses and psychosomatic disorders in the field of psychiatry which has oriented most practitioners to the psychic element in disease and is taking an increasing number of psychiatrists into the private practice of psychiatry as a specialty. The expansion of our mental hospitals due to population increase has called for ever increasing numbers of psychiatrists in such institutions, a field which is of increasing attractiveness because of the many advances in therapeutic techniques. It is estimated there are now some 500 or more psychiatrists and psychiatrists-in-training in Canada.

After World War II it was thought by some of us that a section on psychiatry in the Canadian Medical Association would satisfy the interests of psychiatrists across Canada in these various fields and would enable us to have closer relationships with our colleagues in general medicine and the other specialties. This section held its first meeting in 1946 and has served a very valuable purpose for scientific intercourse.

However, it soon became apparent that there were other features of importance to psychiatrists which could not be served conveniently by such a section, as the sections have no direct authority or power to negotiate except through the Council of the Canadian Medical Association. And although Council has been most gracious and co-operative, nevertheless it could not be expected to have the time to represent Canadian psychiatrists adequately in such problems as the place of psychiatrists in the armed services, relationships with universities, the Royal College of Physicians and Surgeons and the Dominion and Provincial governments, as well as in the development of psychiatric clinics and services in general hospitals and in various other matters, such as medico-legal.

Informal discussions began in 1948 which led to the calling of a meeting of all Canadian psychiatrists in Montreal during the meeting of the American Psychiatric Association in May, 1949. At this meeting an interim committee was set up to ascertain the opinion of Canadian psychiatrists as to the need of an autonomous body and to proceed with plans of organization if opinion was favourable. All Canadian psychiatrists whose names and addresses were available were asked if they would be interested in joining such an autonomous body. The response was almost entirely favourable to such a step being taken.

The interim committee called meetings of Canadian psychiatrists who would be attending the American Psychiatric Association in Detroit in May, 1950 and the Canadian Medical Association in Halifax in June, 1950.

At these two meetings the interim committee was instructed to apply to Ottawa for the incorporation of a body of psychiatrists to be known as the Canadian Psychiatric Association. In this matter the interim committee was ably assisted by Dr. K. G. Gray, who offered to prepare the necessary application forms, and with the help of Dr. John Griffin, to prepare a draft constitution and by-laws to accompany the application. Letters patent, incorporating the Canadian Psychiatric Association, have been issued within the last month.

Application forms for membership have been distributed in recent months to all Canadian psychiatrists. All applications received were dealt with by the interim committee at a meeting held in Montreal on the morning of June 20 and all those approved by the interim committee were accepted as the charter members of

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the Canadian Psychiatric Association.

At the inaugural meeting of the Canadian Psychiatric Association held on June 20, as already indicated, the following officers were elected: President: R. O. Jones, Halifax; Vice-president, C. G. Stogdill, Ottawa; Secretary, J. P. S. Cathcart, Ottawa; Treasurer: R. C. Hamilton, Ste. Anne de Bellevue. The newly elected officers and councillors assumed their respective offices. The Canadian Psychiatric Association has been born and has been launched into the stream of Canadian medical life. May it have a long and useful career.

CLINICAL AND LABORATORY NOTES

EXPERIENCE WITH PLASTIC INSERTS FOR MIDDLE EAR DEAFNESS*

G. ALEXANDER FEE, M.D., *Toronto*

THE USE of various types of artificial drums is as old as otology itself. Most of us have had the experience of improving the hearing in individuals whose drums have been largely destroyed, by small pledgets of cotton sprayed with oil and carefully positioned in the middle ear. Various prostheses have been devised for the same purpose, such as the Leonard ear drum, but they have never been used much by otologists because they were made of rubber and had a tendency to irritate the mucosa of the middle ear and set up a discharge and were difficult to keep in a sterile condition.

Recently Pohlman of California has been advocating the use of small plastic tubes made in different sizes and shapes to be used in this type of patient. Having had some experience with these recently both personally and with a number of patients, I thought it might be worthwhile to present these observations for your consideration.

There are two main types of patients who are suitable; first, those who have had a partial or total destruction of their drum from previous otitis media; secondly, those with radical mastoid cavities. In the case of perforations, the opening must be fairly large, at least 4 mm. in diameter, and must involve the posterior half of the middle ear so that the oval and round windows are exposed to direct view. They must, of course, have a good functioning inner ear as indicated by good bone conduction, and both the stapes and round window must be freely movable. This latter condition is ascertained by the use of an acoustic probe. This is merely a fine bamboo stick tipped with a rounded bead of hard wax, attached to a rectangular piece of thin cardboard. The free end of the sterilized bamboo stick is gently applied to the medial wall of the middle ear, in the region of the oval or round window, while the examiner talks quietly close to the cardboard baffle. If there is a sensitive area the patient immediately notices a marked increase in loudness of the examiner's voice, and an insert is worth a trial. If this test is negative there is no use in proceeding further.

In deciding what size to use, generally with perforations, sizes 1 or 2 are most suitable, while with radical cavities the larger sizes are necessary, *i.e.*, 4 or 5. They do not maintain their position quite as well with radical cavities as they do when there is a rim of drum present. They are most helpful if the ear is dry, but can be worn successfully in the presence of chronic discharge if it is not profuse.

The particular cone shape required in any case depends on the angle of the canal or radical cavity to the sensitive area. I have found D and E most useful. I have tried using inserts with little angulated projecting tails, for cases where the sensitive area was hidden behind or above a rim of drum, but have not found them of any practical value because they are too difficult to get into the right position.

The inserts are not of much practical help in losses greater than 45 db; such people should wear a hearing aid. They are most helpful in losses between 30 and 45 db. At this level they are missing enough to be a constant source of worry and nerve strain, but the loss is not sufficient for them to be willing to accept an electric hearing aid.

The inserts are removed every evening, washed in soap and water, dipped in aqueous zepherin, (1 in 1,000) and put in a small sterile bottle until morning. Most patients can learn very readily how to put them in, in a few seconds, by listening to a running tap or a radio, with the other ear closed.

In suitable cases the improvement is very readily measured on the audiometer by checking the 512 threshold before and after insertion, as most gain is usually obtained at this frequency. There is always a definite improvement of 15 or 20 decibels when the insert is in proper position. Actually, the number of hard-of-hearing people who are of a suitable type to benefit from these inserts is very limited, but to those few they offer very worthwhile and practical help. Learning how to choose the right size and shape in some cases requires practice and patience, but once achieved the pleasure and gratitude of the patient is ample reward for the effort.

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ESCAPE FROM THE BEDPAN

R. H. ROBERTS, M.B., Ch.B.,* *Halifax*

TO NEARLY ALL PATIENTS the use of a bedpan is a horrid, humiliating business and it is astonishing that it has been tolerated so long. Medical men when they become patients are the first to rebel and often insist on staggering through to the toilet though they are unfit to do so. This is one reason why doctors are regarded by the nursing staff as "bad patients" for the "good patient" is one who accepts without protest all the features of hospital life however unreasonable and unnecessary. The doctor as a rule is singularly unsympathetic with the rebellious patient. "Do I *have* to use the bedpan, Doctor?" he is often asked and he will solemnly assure the patient that this is essential knowing full well that in similar circumstances he himself would do almost anything to avoid the indignities of this unphysiological method of going to stool. He is influenced in this attitude by the fact that no satisfactory alternative has been generally available. The use of a bedside commode or of a bedpan placed on a low, hard chair is much pleasanter for the patient but for years the profession has accepted the view that this would involve a greater strain to a sick man and would be more likely to precipitate a vascular accident.

Benton, Brown and Rusk[1] have given the lie to this persistent opinion and their work has proved what many of us have long suspected—that it is in fact much less dangerous for a patient to be helped gently on to a bedside commode than it is for him to mount a bedpan and sit there swaying unhappily "supported" by a spring mattress. The bedside commode itself however is not free from offence and the odour of fæces can linger an unpleasantly long time in wards and private rooms. It also has to be cleaned after use.

Because of these disadvantages we decided to give a trial to the device described by Bohmansson and Malmros[2]—a wheelchair with a perforated seat on which the patient could be wheeled over the toilet pan to defæcate as he sat in a comfortable and physiologically correct position.

A disused wheelchair was stripped of its undercarriage and mounted on a sturdy frame of tubular steel equipped with castor wheels. In the centre of the existing wooden seat a hole was cut and a toilet seat fastened over this. Folding leg boards were fitted to give support when necessary to legs in plaster casts. This completed the conversion and the photograph shows the chair in its final form. Certain points must be kept in mind if such a modification is planned.

(a) The tubular steel undercarriage must of course have no rear axle.

* Surgeon Lieutenant Commander R.C.N., R.C.N. Hospital, Halifax, N.S.

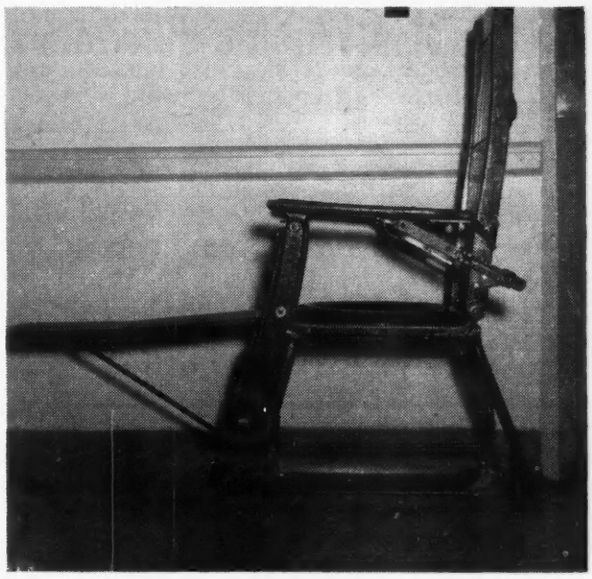

Fig. 1

(b) The rear wheels must be placed sufficiently far backwards to give stability when the patient leans back but must not project so far as to touch the wall before the seat is centred over the pan.

(c) The underside of the seat must clear the upper rim of the highest toilet pan with which it is intended to use the chair. In older hospitals which have been only partly modernized there may be considerable variation in the height of the pans.

(d) The chair must be narrow enough to pass through the narrowest toilet door and to be manœuvred readily in a small room.

The chair has been brought into use at this hospital and has been an unqualified success. The patients are delighted that they can use the toilet in privacy and reasonable comfort, the staff are pleased to have fewer bedpans to wash, everyone is glad to avoid the unpleasant odours of bedpan rounds.

Bohmansson and Malmros described their chair in 1947 and said even then that it was used in most of the Swedish hospitals. I am astonished that this excellent device has not been widely adopted and it is for this reason that I am bringing it once again to the attention of the profession. Existing wheelchairs can be readily adapted to this purpose. We are of course fortunate in having the Naval workshops at our disposal but the conversion I have described is within the capacity of any small machine shop or well equipped garage. At least one surgical supply company* now offers a portable commode chair for sale, and if the demand grows no doubt a variety of models will be made available.

I wish to thank Surgeon Captain A. McCallum, O.B.E., Medical Director General, Royal Canadian Navy for permission to publish this paper.

REFERENCES

1. BENTON, J. G., BROWN, H. AND RUSK, H. A.: *J. A. M. A.*, 144: 1443, 1950.
2. BOHMANSSON, G. AND MALMROS, H.: *Lancet*, 2: 509, 1947.

* McGuire Industries Ltd., Newmarket, Ont.

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(Information regarding contributions and advertising will be found on the second page following the reading material.)

EDITORIAL

CHEST X-RAYS

Controversial problems have come up from time to time concerning procedures in mass chest x-ray surveys and routine chest x-ray examinations in general hospitals. In order to clarify such problems a joint Committee representing the American College of Radiology and the American College of Chest Physicians met in San Francisco on June 26, 1950, and prepared a report. This was subsequently approved by the Board of Regents of the American College of Chest Physicians and by the Board of Chancellors of the American College of Radiology. It is hoped that this report will clarify controversial problems and also that the broad principles upon which it has been formulated may serve as a basis for solving any local situations which may arise.

In this report routine chest survey examinations are defined as examinations conducted on microfilm for screening normal persons to detect the presence or absence of a lesion. They are not to be considered as diagnostic procedures. The 14 x 17″ film is fundamentally a diagnostic tool and its use, therefore, makes the examination more than a screening procedure.

Survey chest x-rays are approved as a screening device if conducted by agencies which utilize well qualified professional technical staffs, and which make a sincere effort to send the positive individuals to qualified local physicians or clinics for proper follow-up. Interpretation and reporting of medical findings is a medical matter and should bear the signature or identification of the responsible physician.

The Committee discourages the reporting of suspicious cases as tuberculosis, believing this to be a clinical diagnosis. It is felt that even the larger film is but one of several examinations necessary in order to establish correct diagnoses.

The Joint Committee believes the radiologist and/or chest physician should be compensated, by arrangement between the physician and the hospital or agency involved, just as any other physician practising his profession. The procedure is time-consuming and places a definite responsibility on the radiologist or chest physician. In the reading of follow-up films there should also be an individual limit to the number of films read in any one day, and this should not be exceeded.

The number of lesions overlooked because of clothing (2%) is considerably smaller than the normal variations of interpretation. Since examination of the fully clothed persons is an easier procedure than that of the undressed persons, the Committee agreed that screening examination of the dressed person is as effective as that of the undressed.

At the present time there is no practical method which could be used to evaluate the qualifications of a particular reader. Studies in this respect are in progress. It is hoped that within a short period of time satisfactory testing methods will be available.

Lastly, the two Committees have agreed that the bi-committee arrangement should continue and another meeting will be arranged in at least one year. In an effort to have the Committees act continuously and without interruption, interim ideas can be sent to the respective Chairmen, and an exchange of opinions will continue during the meeting interval. A.H.N.

Editorial Comments

CHEMOTHERPY

In its accepted modern sense chemotherapy may be defined as the treatment of infections by the chemical action of a drug or compound, which, acting on the infecting organism, so alters its metabolism that it dies or becomes incapable of thriving and multiplying. The former is bacteriocidal while the latter is bacteriostatic. Antibiotics are soluble antibacterial substances produced by moulds and other micro-organisms, when grown upon suitable media. All chemotherapeutic agents are toxic to the patient's tissues as well as the infecting organisms. The usefulness is measured by the chemotherapeutic

index or the ratio of the maximum tolerated dose to the minimal effective dose.

Ehrlich, in 1891, used methylene blue to treat malaria, the first chemotherapeutic agent. The forerunner of the sulfonamides, prontosil, was introduced by Domagk in 1935, since then there has been a continued flow of compounds, some of which have been outmoded.

Pyocyanese, prepared in 1899 by Emmerich and Low, was the first antibiotic, it was too toxic for clinical use, except for local application. In 1929 Fleming noticed the action of penicillin and in 1940 Florey used it to treat staphylococcal infections; since then a new field of medicine has been opened.

Chemotherapy is not a febrifuge treatment and should not be used as such. There is need for cautious thought and investigation before administering chemotherapeutic agents. The type of organism, the state of the patient's blood, the proposed duration of therapy, and the potential toxicity must all be considered. Sulfonamides and/or other chemotherapeutics may be used to confirm a differential diagnosis. Rheumatism is unresponsive to any form of chemotherapy, in fact such treatment is contra-indicated. In a doubtful case—acute rheumatism or acute osteomyelitis of the femur with sympathetic synovitis of the knee joint—an intensive 24 hour course of salicylates will relieve the pain of acute rheumatism and leave the osteomyelitis unaffected.

Ehrlich's theory of "'Therapia magna sterilizans' or Stosstherapie, the giving of a single massive dose sufficient to inhibit any further growth and multiplication of the infecting organism, and leaving the patient's own resistance to overcome the infection by natural phagocytosis," is the most satisfactory method of chemotherapeutic treatment. J.A.S.D.

Dr. Robert M. McFarlane

Our profession contains many who have made their mark in the world of sport, as well as the many, many more who with less distinction but just as much pleasure satisfy their sporting instincts: may it always be so. Occasionally however one man rises to supreme excellence as in the case of Dr. "Bob" McFarlane of the University of Western Ontario. In this part of Eastern Canada at any rate his name has long been amongst the great collegiate footballers, but his even more spectacular supremacy in track events has gained him laurels in national and international circles. To his many awards there now is added the National Amateur Athletic Achievement medal, granted by the National Council on Physical Fitness, for "outstanding achievement in the field of athletics, sports or games, reflecting credit on the nation, and in recognition of a career of good sportsmanship".

It is Dr. McFarlane's fourth such national honour, and we should like to add our felicitations for distinction so finely gained in upholding the best traditions of sport.

ASSOCIATION NOTES

COMMENTS ON THE AMERICAN ACADEMY OF GENERAL PRACTICE

E. C. McCOY, M.D., *Vancouver*

[*Dr. E. C. McCoy of Vancouver, B.C. was sent to the American Academy of General Practice annual meeting in San Francisco as the representative of the General Practitioner section of the C.M.A. and the following is his report as presented to the General Practitioner meeting in Montreal at the annual C.M.A. meeting in June, 1951.*]

In making a report to you of my trip to the American Academy of General Practice (A.A.G.P.), in San Francisco I shall try to be brief—but of necessity shall have to go into considerable detail in places, as I realize that some of you know nothing or at most very little about A.A.G.P.

The day preceding their general meeting there was an all day meeting of the Congress of Delegates which is their business meeting—two delegates from each chapter or state, making a total of about a hundred delegates. This was most interesting and certainly their problems are very similar to ours except that so far they are doing a lot more about them. A report of business transacted would be of no interest to this group—excepting that they have finally ironed out a definition of a general practitioner; he is defined as "a legally qualified doctor of medicine who does not limit his practice to a particular field of medicine or surgery. In his general capacity as family physician and medical advisor he may, however, devote particular attention to one or more special fields—recognizing at the same time the need for consulting with qualified specialists when the medical situation exceeds the capacities of his own training or experience." I believe this definition is very satisfactory and might help us in our thinking.

It was an excellent well organized business meeting and in considering this I'm sure that

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their very excellent general secretary – Mac Cahal, a lawyer, and a good organizer – is the answer. He is a full time well paid secretary and is in a much better position to arrange such a program than are we practising doctors who are too busy in a practice anyway.

Following that all day meeting there were four days of scientific sessions–the best I have ever heard at any convention–by far. The main theme of the convention appeared to be "Family Relations" and the family doctor's part in this, and they had several top-notch men there, *e.g.*, Wm. C. Menninger, professor of psychiatry at the Menninger Foundation's school of psychiatry and at the University of Kansas school of medicine. Also Walter C. Alvarez ex-senior consultant in the division of Medicine of Mayo Clinic and now editor of G.P. the A.A.G.P. journal–a most excellent journal and one to which any of you would find it well worth subscribing. Also Dr. Spurgeon, English Professor of psychiatry at Temple University. There were many other outstanding speakers and I must say one could easily spend 3 to 4 hours talking about them. Suffice it to say that every item on the program was excellent and I particularly liked their arrangement. We had lectures 9 to 10, 11 to 12, 1.30 to 3 and 4 to 5. In other words an hour intermission morning and afternoon which seemed to me a much better idea than the way we suddenly try to make ardent lecture goers out of ourselves and work about eight hours a day as we do in our programs. I think everyone got more out of it and was less tired at the end of the day.

Of course in the evening there were banquets and talent shows, etc. However, I feel that you wanted me to bring back my impressions of what they are doing–what they will accomplish–whether they appear to be going about it in the best way and lastly whether we should be doing something along the same line in Canada.

I should probably first tell you why they formed an organization and how they did it. The organization resulted from a spontaneous movement among groups of general practitioners in a number of states who were convinced that progress and advancement in the general practice of medicine and surgery was basic to the welfare of the people of America and the medical profession. Years before, various groups of specialists had established standards and undertaken programs for the elevation of standards and quality in specialist practice. The specialists established and enforced their own standards. It was felt that the general practitioners should do the same. The trend toward overspecialization was a matter of serious concern among most leaders of the profession and among medical educators. It was felt that the best way to counteract this unhealthy trend was to make better general practitioners who through self-improvement could command the respect of the public and a place of esteem in the profession. It was felt that increased emphasis should be placed on broad clinical training in both undergraduate and postgraduate training. To undertake this an organization was necessary and hence A.A.G.P. was formed. In typical good American style, with about $4,000 in the bank a very progressive group of about a dozen got together and hired a good secretary at a salary of 4 or 5 times their total amount of cash and told him to get the organization going.

They organized apart from the American Medical Association although membership in A.M.A. is a pre-requisite for membership in the Academy, and there is a fairly good working relationship with the A.M.A.–better now than I believe it was at first which I think is good for both sides. At the present time approximately one G.P. in seven in the U.S.A. belongs to A.A.G.P. and they are processing new applications at the rate of approximately 250 per month. There is a staff consisting I believe of seven–including the secretary Mr. Cahal–who handle the business of the Academy. Membership in the Academy costs $15 per year and if one subscribes to their journal that is another $10.

I was most impressed by their Academy and must admit I felt proud to be a general practitioner and in association with such a fine group of men. I believe they are doing what they set out to do and are raising the standards of general practice and as a result increasing the prestige of the general practitioner and giving him some reason for wanting to better himself. Most of us are lazy to a greater or lesser degree and unless we can see some reward either economic or scientific we are inclined to get into a groove–or rut–and stay there.

I certainly gathered the impression that within a very few years one will have to be a member of A.A.G.P. to be recognized as a better type of general practitioner in U.S.A. and quite probably that will become the type of certification there to which we so often refer.

I also feel that what they are doing is good–in other words the foundation is excellent and in my amateurish way of considering this I believe that we cannot hope to achieve anything better than what they have at present. Following this line of thinking to some type of logical conclusion and taking into consideration our present clashing with constitution and by-laws of C.M.A. I fail to see how we can have any organization within the framework of C.M.A. as presently set up which could even start to do what A.A.G.P. is doing. However I still think we should try to work this out within C.M.A. if possible and I believe that a joint committee is now working on that problem.

The whole basis of our organization revolves about the principle of setting up standards, thus making some type of selectivity possible. If we don't have this we might as well quit now–as we will get nowhere in an organization based upon number of men only, thus being an eco-

nomic pressure group. This matter was discussed at great length at executive meeting in Toronto and the above mentioned committee was appointed to try to iron out the basic points of disagreement so that we could achieve selectivity, and if this can be accomplished then probably we can remain a section of C.M.A. and achieve our objectives. I need not discuss this matter further here but will discuss the alternatives.

Prior to going to San Francisco I felt that our 2nd choice if necessary was to form a Canadian Academy and 3rd choice to form a Canadian Chapter of A.A.G.P. The frequent objection you hear to this is that we would be "merely a tail on the American dog" which I believe is a valid objection. However I now feel differently about this and think a 2nd choice would be to form Provincial chapters of A.A.G.P.—one of our provinces about equals some of their states in numbers of G.P.'s. We could thus—if desired—have ten chapters of A.A.G.P. in Canada. I believe this overcomes the objection that we would be merely a tail on the American dog. A 3rd choice would be to form a Canadian Academy. I say this for two main reasons: (1) A Canadian Academy could only be a very 3rd rate one in comparison with A.A.G.P. at best, because of our numbers and our being so spread out in Canada. (2) From an expense point of view, it would be impractical. If today we had in Canada exactly the same number of general practitioners in our organization that they have—that is one in seven—we would have approximately 1,000 and at $15 each that would barely pay a secretary's salary let alone other administrative and travelling expenses. Hence I feel that were we forced to consider alternative 2 or 3 we could get much more for our money by joining A.A.G.P. than by forming a Canadian Academy. Also I believe their organization would benefit from being truly American, that is, pertaining to America and not American as being merely U.S.A.

In conclusion I should say that deep down in my thinking I rather feel that we need both organizations and I think that eventually that may well come, that is, the section of the C.M.A. including all general practitioners looking after our interests from an economic and business point of view and thus maintaining unity; and a second organization, possibly chapters of A.A.G.P., organized from a scientific point of view; in other words a selective organization which would give the men incentive to better themselves and would give them a target to shoot at.

So long as we love we serve; so long as we are loved by others, I would almost say that we are indispensable; and no man is useless while he has a friend.—Robert Louis Stevenson

SECTION OF GENERAL PRACTICE

SYNOPSIS OF HOSPITAL BY-LAWS OF ONTARIO

GLENN SAWYER, M.D., *St. Thomas, Ont.*

[The following synopsis has been prepared by Dr. Glenn Sawyer of St. Thomas, Ont. These by-laws have been accepted by the Ontario Medical Association and the Department of Health, Province of Ontario. The extent to which they have yet been implemented varies, but their recognition throughout the province is to be considered of the greatest importance in improving the status of the general practitioner.

These by-laws are indispensable, but it must always be remembered that they provide for no privilege without accompanying responsibility.—EDITOR.]

At the annual meeting of the Section of General Practice of the Canadian Medical Association, held in Montreal on June 23, 1951, I was asked to prepare a brief synopsis of the hospital by-laws of Ontario as they affect the general practitioner.

In the formation of any hospital by-laws consideration must be given to several things.

1. A set-up whereby the hospital facilities are made available to all those who wish to abide by the by-laws of the hospital concerned.

This is accomplished by dividing the staff into Honorary, Consulting, Active, Associate and Courtesy groups. The Active Staff is then divided into departments such as medicine, surgery, obstetrics, gynæcology, general practice, radiology, pathology, anæsthesia, etc.

General Practice is an administrative department and patients are not admitted to it. Members of the general practice department apply for privilege in one or more of the other departments. However the chief of the general practice department sits on the medical and surgical advisory committee and members of the department sit on all standing and special committees.

This type of department is valuable to the general practitioners in two ways: (a) By changing departments from year to year he can increase his general knowledge and hence become a better all-round general practitioner. (b) A general practitioner, wishing to become certified in any particular branch of medicine, may remain in that department and seek increased privilege as his competence increases.

The other divisions of the staff have their usual significance. New members of the staff, who wish to become members of the active staff, are placed on the associate staff. They apply for privilege in a department and are assigned as juniors to the members of that department. They have all staff privileges except that they cannot vote or hold office. They may be elevated to the active staff by the credentials committee.

2. There must be a method of granting and controlling privilege.

It is essential that the work within any hospital is under the control of the members of the

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staff of that hospital. This has been accomplished by the formation of two committees.

A. *The Credentials Committee.* — This committee is composed of five members of the acting and consulting staffs. It shall appoint its own chairman. To give continuity, at the outset, two members shall be appointed for one year, two for two years, and one for three years. Thereafter all appointments shall be for three years.

Duties of the Credentials Committee: (1) To consider applications for membership—to investigate each fully and recommend the department for each and the amount of privilege. (2) To consider requests for change from one department to another. They may also, on their own, so recommend a change. (3) To act as a nominating committee.

B. *The Medical and Surgical Advisory Committee.*—This committee is composed of the staff executive and the chairman of each department. This group then elects a chairman who is chief of staff.

The general staff elects an executive which is composed of a President, Vice-President and Secretary. The executive is responsible for the administrative side of staff affairs. This will include such things as records, interns, pharmacy and nurse education. The President presides at all staff meetings; he is ex-officio a member of all committees and represents the staff on the Board of Governors. In his absence the Vice-President shall possess his powers, perform his duties and represent the staff on the Board of Governors. The Secretary shall act in that capacity for the general staff and also for the Medical and Surgical Advisory Committee.

The chief of each department is elected by the members of that department. They, together with the chief of staff, are responsible for the clinical side of staff affairs. This responsibility includes both staff and private patients.

In the granting and control of privilege the Medical and Surgical Advisory Committee have the final decision, based on recommendations of the Credentials Committee.

In small hospitals the Executive acts as the Medical and Surgical Advisory Committee. The President acts as the chief of staff and also represents the staff on the Board of Governors. If the staff becomes divided into departments the chief of each department also sits on the committee.

COMMENT

These By-Laws are by no means complete. However, so far as the general practitioner is concerned, they do several things: (1) They provide a method whereby the general practitioner may become a member of the active staff. (2) They give the general practitioner an adequate voice in the administration of staff affairs. (3) They allow the general practitioner the privilege of day to day postgraduate study under the specialists of his own hospital.

Copies of the complete By-Laws for intermediate and smaller hospitals may be obtained by writing the Secretary of the Ontario Medical Association at 135 St. Clair Ave. West, Toronto 5, Ontario.

ANNUAL MEETINGS OF AFFILIATED SOCIETIES

IT IS WITH CONSIDERABLE SATISFACTION that we are able to report that the following societies which are affiliated with the Canadian Medical Association will meet in conjunction with the Eighty-third Annual Meeting at Banff-Lake Louise.

Society of Obstetricians and Gynæcologists of Canada, June 6 to 8, 1952, Banff Springs Hotel.

Canadian Neurological Association, June 8 and 9, 1952, Banff Springs Hotel.

Canadian Society of Anæsthetists, June 9 and 10, 1952, Banff Springs Hotel.

Canadian Association of Pathologists, June 9 and 10, 1952, Banff Springs Hotel.

Canadian Association of Radiologists, June 9 and 10, 1952, Banff Springs Hotel.

Canadian Rheumatism Association, June 9 and 10, 1952, Banff Springs Hotel.

Canadian Academy of Allergy, June 10, 1952, Banff Springs Hotel.

Canadian Pædiatric Society, June 9 and 10, 1952, Chateau Lake Louise.

Canadian Heart Association, June 10, 1952, Chateau Lake Louise.

Canadian Medical Protective Association, June 12, 1952, Banff Springs Hotel.

Members of these societies will learn further details of the programs from their own officers. All housing arrangements are in the hands of the Committee on Housing of the C.M.A. and members are urged to apply at an early date, utilizing the form published elsewhere in this issue and mentioning the name of the society whose meeting they plan to attend.

MEDICAL SOCIETIES

Nova Scotia Division, Annual Meeting

Under the direction of President J. J. Carroll the Nova Scotia Division of the Canadian Medical Association held its ninety-eighth annual meeting at Antigonish on September 10 to 13. Following the trend of recent years the business problems of the society loomed great and took more time and discussion while matters clinical and scientific, though prominent and well presented took secondary places in the lobbies, private discussions and bull sessions which went on into the night, as well as in the auditorium.

Antigonish, host for the first time in more than twenty-five years was an ideal setting. The weather was balmy

and the many halls, converted committee rooms, dining hall and residences of St. Francis Xavier University gave the members greater scope than they have had for a long time.

Present at the meeting as distinguished guests were the congenial C. M. A. President Dr. H. B. Church; the ubiquitous and ever welcome Deputy General Secretary, Dr. Kelly; Dr. H. M. Coleman, Toronto orthopædic surgeon; Dr. Carleton B. Pierce, McGill Professor of radiology; Dr. Glenn Sawyer of St. Thomas, Ontario, speaker on the problems of general practice; and Dr. E. M. Worden of McGill Department of Pædiatrics. Supporting the visitors in the scientific part of the program were Dr. Martin Hoffman, Dalhousie Professor of Clinical Research; Dr. Graham Simms, Chairman of the Health Committee of Provincial and Civil Defence; and Mr. C. R. Ross, industrial hygiene engineer of the Nova Scotia Department of Public Health.

Often the dull facet of such a gathering, the committee reports, by their outstanding quality, the obvious study, labour and executive ability which had gone into them, were the outstanding features of the meeting, pointing up again the fact that medical men are taking more seriously than ever before their obligations as a group to society. The advisory committee on the distribution of federal health grants, the cancer committee, the committee on industrial medicine, the economics committee and many others submitted reports embracing their fields in a most comprehensive manner.

Among the recommendations of the society were that the postgraduate committee of the Dalhousie Medical School, whose work received high praise, be asked to put on a refresher course in industrial medicine; that the tenure of office of the President of the Provincial Medical Board be limited to three years; that no action at present be taken on the request of the Maritime Hospital Association for nominees from the society as governors; that the economics committee be instructed to negotiate with the federal government regarding arrangements for the treatment of welfare group patients and blind pensioners; that the government is asked to set up forty beds for the investigation and care of arthritic problems; that the action of the Pictou County Medical Society in branding the Registered Nurses Association Bill known as the *Registered Nurses Association Act 1950* as discourteous to the medical profession was sound. This bill, passed without consulting the profession, involves increased teaching responsibilities on the part of provincial medical men in nursing schools. The profession-sponsored Maritime Medical Care was discussed widely and often critically with perhaps not sufficient appreciation of the difficulties through which any such scheme must pass during its formative period.

Dr. Carroll's presidential address dwelt with the social problems of medicine. He spoke of the merits of the medical care of the welfare group despite the difficulties in its administration. He stressed the importance of some check on the uses of such a service. He reviewed the present standing of Trans Canada Medical Services, emphasizing the value of such a scheme and the importance of co-operation which must be not only geographical but be the concern of every patient as well as hospital and doctor.

Membership of the Nova Scotia Division for 1951 was given at 466 of whom 448 were conjoint members, 17 honorary members, 1 member of the Nova Scotia Division only.

Dr. L. M. Morton of Yarmouth was elected as President of the Nova Scotia Division for 1951-52. Vice-Presidents are Dr. J. W. Reid, Halifax, and Dr. M. G. Tompkins, Dominion. Dr. H. G. Grant of Dalhousie Medical School was re-elected Secretary and Dr. R. O. Jones of Halifax as Treasurer. ARTHUR L. MURPHY

University of Toronto

The Physiological Society of the University of Toronto heard Dr. Sune Bergstrom, University of Lund, Sweden, on "Intestinal Absorption and Distribution of Fatty Acids and Glycerides in the Rat" and Dr. Gerhardt von Bonin, professor of Anatomy, University of Illinois on "Functional Organization of the Cerebral Cortex" in October.

Mr. J. C. D. Barlow, department of physiology, spoke on "The Treatment of Experimental Anuria by Intestinal Perfusion" in November.

Ontario Medical Association

District No. 6 met at Peterborough October 16 and 17. Dr. W. G. Cosbie spoke on "Cancer of the Uterus". Dr. C. L. Ash spoke on "X-ray and Radiotherapy of Interest to the General Practitioner". Dr. K. J. R. Wightman spoke on "Recent Advances in Therapeutics." Dr. Roy H. Malyon president-elect was the guest speaker at lunch.

District No. 7 met in Kingston October 18. Dr. A. M. Bryans, Kingston, spoke on "Recent Advances in Pædiatrics". Dr. James A. Dauphinee, Toronto, spoke on "Radioactive Isotopes and Their Present Use".

District No. 4 met at Hamilton October 23 and 24. Speakers were Dr. Benson Rogers on "Digitalis Intoxication"; Dr. Charles Jaimet on "Thrombocytopenic Purpura"; Dr. Allan Kennedy on "Acute Cardiac versus Pulmonary Lesions"; Dr. Adrian Yaffe on "What Symptoms Mean Heart Disease"; Dr. Keith Stuart on "Hypothyroidism"; Dr. Francis Ruston on "Cardiac Arrest in O.R."; Dr. Albert Pain on "Management of Breech Presentation"; Dr. R. T. Weaver, on "Gynæcological Emergencies in General Practice"; Dr. Vaughn Renshaw "Emergency Treatment of Burns"; Dr. A. K. Mighton on "Emergency Treatment of Hand Injuries"; Dr. Donald Campbell on "Investigation of Rectal Bleeding"; Dr. J. F. Brunton on "Treatment of Renal Infection". The staff of Mountain Sanatorium gave a symposium on Tuberculosis. Dr. Francis Brien, London, was the dinner speaker. His topic was "Out of the Frying Pan into the Fire".

District No. 1 met at Sarnia November 6 and 7. The members were addressed by a team of speakers from the Crile Clinic, Cleveland, Ohio. The dinner speaker was Professor James Talman, Lawson Memorial Library, University of Western Ontario. LILLIAN A. CHASE

CORRESPONDENCE

Aureomycin in Amœbic Dysentery

To the Editor:

I am a medical missionary and my field of labour is in Angola, Portuguese West Africa. Like most of my colleagues who serve on the health frontiers of the world, when I return to Canada on furlough it is to learn all that I can and to get "*caught up*" with the seemingly endless new developments in Medicine and Surgery in the homeland.

Today I have been reviewing the recent literature on Amœbic Dysentery. I find many favourable references to aureomycin but I feel that the dramatic results which this antibiotic achieves in acute amœbic dysentery might be even more strongly emphasized. I have been seeing and treating amœbic dysentery for twenty years under conditions where perforce one's aim must be simply the clinical cure of the disease in the shortest space of time with the least possible treatment and, if possible, at modest cost.

During the past year I have treated some twenty-five cases of clinical amœbic dysentery with aureomycin. In all of them there were active trophozoites, cysts or precystic forms of *amœba histolytica* in the stools. All of the

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patients were suffering from the usual symptoms of amœbic dysentery and at least half of them were severe cases of the disease. In all these cases there was considerable or complete relief of symptoms within twenty-four hours. Three days was the longest time that was necessary to achieve a clinical cure. All of the patients had passed at least one stool free from amœbæ by the end of this period. Follow-up stool examinations for parasites was not feasible. Adult dosage was one-half gram every six hours.

From my experience in the treatment of amœbic dysentery under primitive conditions, aureomycin appears to be the most valuable weapon now in our armamentarium.

W. SIDNEY GILCHRIST
29 Kaye St.,
Halifax, N.S.

New Method of Setting a "Colles' Fracture"

To the Editor:

A Colles' fracture is of very common occurrence and the usual method of treatment often results in considerable deformity and more or less permanent disability due to imperfect reduction of the lower fragment of the radius. This reduction is often very difficult especially if the fracture is impacted. I thought perhaps other medical men might wish to adopt a method of reduction which I discovered some time ago and found very effective.

The method is as follows: Place the patient on an ordinary operating table and give a general anæsthetic to relax the muscles. Near the head of the table place a chair, on which the surgeon, facing the head of the patient, places his left foot. He then brings the arm to be set across his flexed left knee and uses the latter as a fulcrum to reduce the fracture. He must use both hands forcibly on the lower fragment until he feels it move forward and downward into correct position. A suitable splint is then applied with the hand everted.

When reducing a fracture of the left arm the surgeon stands facing the head of the patient on the left side and for those of the right arm he stands on the right side and faces the feet of the patient.

W. H. LANG
Vancouver, B.C.

SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

THE NEW GOVERNMENT

Politics and medicine make uneasy bedfellows. The settling-down process since the inauguration of the National Health Service has not been facilitated by the personality of the Minister responsible for health during the greater part of this time. His successor, in view of the imminence of a General Election, was obviously only a stop-gap appointment, and he never had the opportunity to leave his imprint upon the Ministry of Health. There is therefore widespread pleasure throughout the medical profession at the prospect of having a non-socialist as the Minister of Health. So much requires to be done to "streamline" the Service that obviously no socialist Government was prepared to tackle it. There is no question of repealing the Act establishing the National Health Service, but much can be done to humanize it and to ensure that the maximum efficiency can be obtained at the minimum cost. There is no good reason why the country should not, under the new régime, acquire a first-class medical service with an adequately remunerated medical personnel at a cost lower than that already authorized by the Treasury and Parliament. The new Minister of Health has a great opportunity of restoring to the practice of medicine some of its pristine glory, and he carries into office the best wishes of the entire profession.

REFORM OF THE HEALTH SERVICE

It is a fortunate coincidence that the publication of the first of a series of reports by the Council of the British Medical Association, incorporating recommendations for the reform of the National Health Service, should have coincided with the change of Government. Many of the recommendations are aimed at modifying the powers to make regulations and orders, at present possessed by the Minister of Health. In the National Health Service Act there are no fewer than 40 clauses which confer such powers upon the Minister. This may make for flexibility, as has been argued in the past, but there are many who are not happy at the possible abuse inherent in the possession of such powers by a Minister.

Other recommendations include sweeping reforms in the organization of the hospital service, whilst others again deal with specific points. Two in this last category may be mentioned. One, aimed at maintaining facilities for private consultant practice, is that it shall be obligatory upon the Minister to provide adequate pay-bed accommodation at a reasonable charge, and that patients, in virtue of their rights to free hospital accommodation, should be allowed a grant-in-aid for accommodation in a private bed. The other recommendation is that patients obtaining their medical care privately should be allowed to obtain their prescribed drugs and appliances at the public expense. This penalizing of the patient who preferred to pay his doctor's fees was one of the most vindictive features of the National Health Service Act.

A NOTABLE OCTOGENARIAN

The name of Sir Robert Hutchison, Bart, is synonymous with all that is best in pædiatrics in this country. To celebrate his 80th birthday, which fell on October 28, the October issue of the *Archives of Disease in Childhood* has been published in his honour. One of the many truants from the Edinburgh School of Medicine, it is fifty-five years since he first migrated to London, and over fifty years since he was appointed to the staff of the Hospital for Sick Children, Great Ormond Street, London. Although he entered into a great tradition, initiated by Thomas Barlow and Frederick Still at Great Ormond Street, and John Thomson in Edinburgh, he enhanced it still further and he is now universally recognized as the father of pædiatrics as we know it in this country today. His influence owes much to his gift for writing and teaching. His fourteen books range over nutrition, treatment, and clinical methods, as well as pædiatrics, but it is those in this last category which show him at his best. He had a genius for lucid explanation which was enlivened by that caustic wit of his which has been famous for many years. It is safe to say that there is not a generation of students during the last fifty years, irrespective of their medical school, which has not imbibed much of Hutchison's teaching, either by word or mouth or from his books. "Bobby Hutch", as he was affectionately known by many, is already a tradition in British medicine. It is the sincere wish of all his innumerable friends—former patients, students and colleagues—that he will long be spared to enjoy that retirement which he has so richly earned.

A MEDICAL CENTENARIAN

Medicine compares badly with the Church where longevity is concerned. Last month, however, witnessed the attainment of his 100th birthday by one of the prominent physicians of his day—Dr. Clifford Beale, who was born in Birmingham on October 16, 1851. After qualifying at Guy's Hospital, he was duly appointed to the staff of the City of London Hospital for Diseases of the Chest, and of the Great Northern Central Hospital (now the Royal Northern Hospital). He has been a

Fellow of the Royal College of Physicians for over sixty years and he is the oldest member of the British Medical Association. He collaborated with Sir Clifford Allbutt in the revision of the section on diseases of the circulatory system in the fourth edition of the "Nomenclature of Disease", published by the Royal College of Physicians in 1906, and, among his many writings, was a textbook on "The Treatment of Pulmonary Consumption: A Practical Manual", written in collaboration with Dr. V. D. Harris, and published in 1895. Outside his speciality—disease of the lungs—he was a keen advocate of hospital reform.

WILLIAM A. R. THOMSON

London, November, 1951.

OBITUARIES

DR. CHARLES BUCKINGHAM, former Toronto General Hospital and Toronto Sick Children's Hospital surgeon, died recently. He was 81. He had served as associate professor of surgery and medicine on the faculty of the University of Toronto Medical School.

DR. ELDON DURWARD BUSBY, aged 57, died recently at his home in London, Ont. He had been ill with a lung ailment for six months. In May, he underwent an operation in Ann Arbor, Mich., and returned to London in August to resume his practice. Dr. Busby was professor of urological surgery at University of Western Ontario Medical School and Victoria Hospital, and consultant in surgery at Westminster Hospital and Beck Memorial Sanatorium. Born in Southampton, November 16, 1894, Dr. Busby spent his early years in the Yukon, where his father was an official with the Canadian Customs. He moved to Vancouver with his family in high school days, and later attended McGill University in Montreal, receiving his Bachelor of Arts degree in 1913. From there he went to Harvard, where he graduated in medicine in 1917. He joined the Harvard Surgical Unit immediately upon graduation and proceeded overseas as a lieutenant. He was a fellow of the Royal College of Surgeons of Canada and the American College of Surgeons. For many years he represented the university on the Medical Council of Canada. Dr. Busby was a member of Metropolitan United Church and the Rotary Club.

Surviving are his widow, a son, Dr. Stuart M. Busby, of London who will be carrying his practice at his father's address in London, one daughter and two brothers.

DR. OLIVE GAIR PATTERSON CAMERON, aged 66, died in Toronto on Sept. 18. A lifelong resident of Toronto, she was the wife of Dr. Malcolm H. V. Cameron. A graduate in medicine from the University of Toronto in 1916, she was associated with the bio-chemistry department. She was a life fellow of the Academy of Medicine and an officer in the University Women's club. She was a member of St. Andrew's United Church. Surviving are her husband and three sons.

DR. JOHN FERGUSON DOYLE, aged 66, died in Kingston, Ont., following a short illness. Born on Garden Island, he spent the greater part of his life in Tweed and was an active practitioner there from 1918 until his retirement a year ago. He had lived in Kingston since then. Active in the Holy Name Society and the Knights of Columbus, Dr. Doyle attended St. Mary's Cathedral since moving to Kingston. He leaves his widow and two sons.

DR. JOSEPH APPELBE GILCHRIST, aged 58, the first walking diabetic patient to receive insulin treatment, died on Sept. 26 of a coronary thrombosis. Contracting diabetes while training with the C.A.M.C. at Toronto during the First World War, Dr. Gilchrist specialized in diabetes and was a personal friend of Sir Frederick Banting. Born at Brantford, Dr. Gilchrist graduated in arts and in medicine in 1916 from the University of Toronto. Following the war he served until 1925 at Christie St. Hospital. He was formerly a member of Lambton Golf Club. He was a member of various medical societies and the Masonic Order. He leaves his widow.

DR. JOHN GOURLAY, aged 48, died on September 18 in Barrie, Ont. Coming to Canada from Glasgow, Scotland, at the age of two, he received his early education in Toronto, later attending University of Toronto. After graduating, he worked in Toronto, moving to Barrie seven years ago. During the war he was a Captain in the R.C.A.M.C. stationed at Camp Borden. Surviving him are his widow and a daughter.

DR. DONALD MACLAUCHLAN, aged 92, of 1026 14th Ave. W., died in Calgary on September 9. He was born in Charlottetown, P.E.I., where he taught school for several years before entering Trinity Medical School in Toronto. He graduated in 1886 and moved to O'Leary Station, P.E.I., where he practised for 14 years. In 1912 he came to Calgary, where he practised medicine until retiring in 1949. He is survived by his widow, two sons and four daughters. Dr. MacLauchlan was an active member of Grace Presbyterian Church, the Masonic Order, the Odd Fellows, the Sons of Scotland, and Canadian Order of Foresters.

DR. GEORGE K. MACNAUGHTON, aged 74, died on September 15, at Cumberland, B.C. One of Vancouver Island's best known physicians and surgeons, he was Conservative member for Comox in the B.C. Legislature from 1928 to 1933. He was born in Black River, N.B., was graduated from McGill University in 1906, and arrived in Cumberland the same year. In 1912 he was appointed medical officer for Canadian Collieries (Dunsmuir) Ltd. and member of the hospital board, and held the positions until his death. He was also a prominent Mason, founded the Canadian Club in the district, and served the St. John Ambulance Association for many years. Surviving are his widow and a daughter.

DR. JOHN BRUCE McGREGOR, aged 65, died Sept. 14 at Saskatoon Hospital. Dr. McGregor was born at Welland and graduated from Manitoba Medical College. At the time of his death, Dr. McGregor had held the position of Pensions Medical Examiner for the Department of Veterans' Affairs for 10 years. Dr. McGregor won the Military Cross for service during the First World War. At Kerrobert he was at one time president of the Canadian Legion; Worshipful Master of the Masonic Lodge and a shriner. He was also on one occasion president of the Liberal Association there. He is survived by his widow, a son and a daughter.

DR. JOHN RANKINE died in Halifax on September 19. Born in Port Glasgow, Scotland, he was 69 years old. He came to Halifax in 1888 and graduated at Dalhousie University. He had practised medicine in Halifax since his graduation in 1904, except for a period overseas with the Dalhousie contingent. As a young man, Dr. Rankine was an outstanding athlete, particularly gifted in football and track. He was captain, later coach of the Dalhousie University football team. A brother survives him.

DR. OPIE SISLEY, aged 89, died in Toronto on Sept. 16. He was born in Scarboro Township and graduated from the University of Toronto in 1887. He established a practice in Agincourt, where he remained for 17 years. Keenly interested in politics, he was a member of the Ontario Liberal Association and active in election campaigns. Dr. Sisley was an enthusiastic bowler in his younger years and a member of the Balmy Beach Bowling Club. He was also a member of Emmanuel Presbyterian Church. He leaves a son and a daughter.

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THE STATE OF THE NATION

A. D. KELLY,
Deputy General Secretary

The vitality of the Association's provincial divisions continues to gain strength.
There is a growing local interest in both technical and non-technical affairs of the divisions.
There is active co-operation by doctors in the development of prepaid medical plans, and support for Trans-Canada Medical Services.
Through the sustained efforts of the profession, hospital and other medical facilities are expanding as doctors set their sights on the highest standards of medical service.

These are the conclusions which may be drawn as a result of the divisional meetings recently held across the country. One of the responsibilities, and privileges, which the Canadian Medical Association imposes, or confers, on its president, is an official visit to each of the 10 divisional annual meetings, accompanied by a member of the Secretarial staff.

Dr. Harcourt B. Church, accompanied by the writer, has attended in quick succession eight divisional meetings from August 28 to October 12. Truly our president has been "on call" in the interest of the medical profession and the people whom we serve.

One would be dull indeed if such an experience did not convey a better appreciation of the Canadian scene and the part which our profession is playing in the building of the nation. Canada is literally bursting at the seams in an era of rapid growth and development. Economically and sociologically this expansion is evident from the Atlantic to the Pacific and, like all growth phenomena, it is accompanied by necessary changes and adjustments.

In the field of medicine one sees new and energetic attacks on the age-old problems of cancer, arthritis and tuberculosis. It is encouraging to observe the partnership between the official health agencies and practitioners of medicine in meeting these menaces to the health of our people. The bricks and mortar of recent additions to hospital facilities of the nation are evidence of expansion. New medical schools will shortly be graduating additional recruits to the ranks of the profession and in their development there is abundant proof of the sound planning which is so essential to these fundamentally important institutions.

In the business sessions of the divisional meetings there was much discussion on methods of distributing medical services. Our plans of prepaid medical care are gaining widespread public acceptance and their growth in most instances is as rapid as administrative practices will permit. The formation of Trans-Canada Medical Services is regarded as a forward step. But the inherent promise of this new organization must shortly be justified by its performance in spreading the benefits of prepaid medical care coverage. Any tendency to complacency at the growth of our plans is tempered by an awareness on the part of the profession that they have to date made little progress in covering rural subscribers and providing contracts for individuals. The medical care of the large new group of recipients of old age pensioners was thoroughly discussed and the policy of the Association was everywhere reaffirmed—that these pensioners are not automatically entitled to government-sponsored medical care.

Much interest was displayed in the operation of the National Health Service in Great Britain and in the Canadian evidences of the trend to government intervention in medical care. Critical as we are of the shortcomings of the British scheme, and convinced that it is quite unsuitable for Canada, we must lose no time in demonstrating that our own voluntary approach to the problem of budgeting for the cost of medical and hospital services is a better alternative. Although the large majority of our profession is convinced that we can do so our position is weakened by two attitudes displayed by some of our members. The first and most dangerous viewpoint is represented by the doctor who ignores the signs and who assumes that the comfortable ways of private practice will persist unchanged. To him "socialized medicine" is unthinkable and he belittles the efforts of the profession to promote plans of voluntary prepaid medical care. He is a menace to endeavour because he believes that "It can't happen here". At the other end of the scale, a few of our people assume that despite our best efforts, eventual domination of the practice of medicine by government is inevitable. This defeatist attitude leads them to stop struggling to promote and improve our voluntary plans and they have already thrown in the sponge.

Fortunately, the profession as a whole adopts neither of these attitudes. Attuned to the times and playing its full part in Canada's growth and development, it recognizes the need for promoting a distinctively Canadian approach to the health problems of our restless people. The profession does not deny the place of the state in the promotion of health services and it believes that it has demonstrated its ability to work in harmony with governments to the great advantage of all Canadians.

The presidential tour provided an excellent opportunity to assess the vitality of our organiza-

tion and its constituent Divisions. Beginning at the meeting of the infant Newfoundland Division at St. John's, it was immediately evident that the doctors of our newest province have been stimulated and aided by their contact with the national Association. In this area with its unique medical problems, Confederation has had the effect of initiating such public services as Workmen's Compensation. The profession is considering its relationship to this and other matters, familiar to the profession elsewhere.

The New Brunswick Division met in the delightful surroundings of the Algonquin Hotel at St. Andrews, at its seventy-first annual meeting. The smoothness and efficiency with which the sessions were conducted testify to the experience gained in contributing to the medical life of the province and the country as a whole over such a long period.

The real veteran of organized medicine in Canada, our Nova Scotia Division assembled for its Ninety-eighth annual meeting at Antigonish. The facilities of St. Francis Xavier University were placed at our disposal and a diversified program of business, scientific and social events was presented.

The vigour of the Island Division was never better displayed than at this year's meeting at Charlottetown. Panel discussions on cancer control and on the Mental Health Program were convincing demonstrations of the integration of the division with the immediate problems of its province. The business sessions showed that the doctors of P.E.I. are well informed on the issues of the day.

At these four Maritime meetings a single team of speakers accompanied the president and made most effective presentations to the scientific sessions. The Canadian Medical Association and its divisions are grateful to these busy practitioners and teachers who contributed so much to the educational activities which are fundamental to the purposes of our organization. It is encouraging, however, to note that our divisions are not now depending solely on guest speakers to provide the educational program. Presentations by local contributors are finding an increasingly important place.

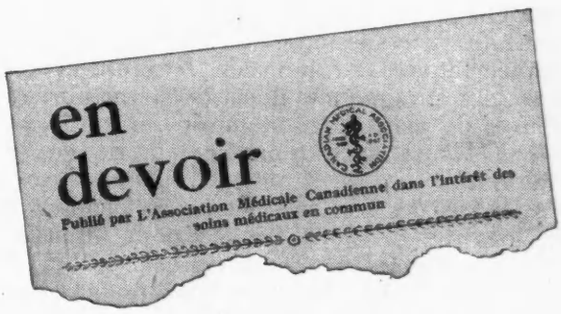
The scene quickly changed to the west where the first of four meetings was convened by the Saskatchewan Division at Moose Jaw. Despite the coincidence that the duck shooting season opened the same day, a large attendance of Saskatchewan doctors and their wives was registered. Business, scientific and social activities were pursued with the enthusiasm characteristic of our Saskatchewan colleagues and here the contribution made by local speakers to the scientific program was outstanding.

Next, the forty-sixth annual meeting of the Alberta Division was held at Edmonton. Here the stimulating atmosphere of Canada's oil capital and the stabilizing influence of the University of Alberta were evident. Although actively engaged in many important intra-provincial medical projects, our Alberta friends found time to discuss plans for the Eighty-third annual meeting of the C.M.A. which will be held at Banff and Lake Louise during the week of June 9, 1952. Dr. Harold Orr, president-elect, and his local committees are making preparations for a memorable gathering.

The British Columbia Division assembled at Vancouver for a week of diversified activity including the official opening of the new home of the Vancouver Academy of Medicine. This modern building provides ample accommodation for the medical library as well as office and committee rooms for all provincial medical organizations. Its facilities created a feeling of envy among the visitors who inspected it. A momentous decision was reached at this meeting and the B.C. Division will undertake to finance its own activities by levying an annual fee among its members on a voluntary basis.

The final meeting on the presidential tour was that of the Manitoba Division at Winnipeg. Well documented and well arranged, it provided a fitting climax to a highly informative survey of Canadian medicine from coast to coast.

Although it is fallacious to draw conclusions relative to the state of an organism as complex as the Canadian medical profession, it is possible to report the impression that the subject is alive and vigorous, even lusty, and that in this respect its condition parallels that of the nation.



LA SITUATION AU PAYS

A. D. KELLY,
Sécrétaire Générale Suppléant

La force des Divisions provinciales de l'Association continue de grandir.

Il existe un intérêt local grandissant dans les affaires techniques et non-techniques au sein des Divisions.

Il existe chez les médecins, une coopération active à l'égard du développement des plans médicaux pour les soins payés d'avance, et un soutien précieux en faveur des service médicaux trans-Canada.

Par l'entremise des efforts soutenus par la profession, les hôpitaux et les autres organisations médicales se répandent de plus en plus tandis que les médécins établissent encore mieux leur position en faveur des plus hautes exigences du service médical.

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Voilà les résultats qui peuvent être conclus à la suite des réunions tenues par les divisions à travers tout le pays. L'un des devoirs et privilèges qui incombent au Président de l'Association Médicale Canadienne, comprend une visite officielle à chacune des dix réunions annuelles tenues par les divisions, où celui-ci est accompagné par un membre du sécrétariat.

Le Dr Harcourt B. Church, accompagné du rédacteur de cet article, a assisté, entre le 24 août et le 12 octobre, à huit réunions successives parmi les divisions. Réellement, notre Président s'est dépensé beaucoup dans l'intérêt de la profession et des gens que nous servons.

Il serait triste de constater une telle expérience si elle n'apportait pas avec elle une meilleure appréciation de la situation au Canada et si elle ne témoignait pas en faveur du rôle que notre profession joue dans le développement de notre nation. Le Canada vit actuellement une période de progrès très actif et se développe beaucoup. Aux points de vue économique et sociologique, ce développement s'affirme de l'Atlantique au Pacifique, et comme tout phénomène de croissance, celui-ci s'accompagne de changements et d'ajustements nécessaires.

Dans le champ de la médecine, l'on peut voir surgir des solutions nouvelles et énergiques pour résoudre les vieux problèmes du cancer, de l'arthrite et de la tuberculose. Il est encourageant de constater les efforts combinés des organismes officiels de santé et des médecins, pour combattre ces menaces au bien-être de notre peuple. Les nouvelles constructions récemment ajoutées aux hôpitaux du pays, constituent un témoignage de ce développement. Des écoles médicales nouvelles offriront bientôt des recrues supplémentaires au rang de la profession, et dans leur programme il existe de nombreuses preuves de plans bien organisés qui sont essentiels à l'importance fondamentale de ces institutions.

Au cours des sessions techniques pendant les réunions des divisions, beaucoup de discussion a eu lieu sur les méthodes de distribution des services médicaux. Nos projets relatifs aux soins médicaux payés d'avance sont de plus en plus acceptés favorablement par le public et leur développement dans la plupart des cas est aussi rapide que les exigences administratives le permettent. La formation de services médicaux Trans-Canada est considérée comme un grand pas en avant. Mais la promesse inhérente à cette nouvelle organisation doit être justifiée bientôt par une réalisation plus définie et par une répartition plus étendue des bénéfices apportés par les soins médicaux payés d'avance. Au stage de développement de ce projet, les conditions ne sont pas satisfaisantes par suite de l'attitude démontrée par la profession qui ne réalise pas le peu de progrès accompli pour répandre cette organisme parmi la classe rurale, et pour fournir des contrats pour les individus. Les soins médicaux à donner au nouveau groupe considérable de ceux qui reçoivent la pension de vieillesse, ont été discutés à fond, et la ligne de conduite de l'Association a été partout ré-affirmée de nouveau—à savoir que ces bénéficiaires de la pension n'ont pas automatiquement droit aux soins médicaux sous l'égide du gouvernement.

Beaucoup d'intérêt a été manifesté à l'égard du fonctionnement du Service National de la Santé en Grande-Bretagne, et à l'égard de la situation au Canada relative à l'intervention du gouvernement dans les soins médicaux. En considérant d'un œil critique les points faibles du système adopté en Grande-Bretagne, et convaincus que ce système ne convient pas au Canada, nous ne devons pas perdre de temps pour démontrer que notre participation volontaire dans la résolution de ce problème, en nous occupant des questions budgétaires concernant les médecins et les hôpitaux, est une alternative préférable. Cependant, bien que la majorité des membres de notre profession croient que ce fait est possible, notre position est abaissée par deux attitudes que démontrent certains de nos collègues. La première attitude est la plus dangereuse et représente le médecin qui ignore les augures et qui prétend que les conditions confortables de la pratique privée persisteront à ne pas changer. Pour lui, la "médecine étatisée" ne vaut pas la peine d'y penser, et cette attitude amoindrit le travail de la profession qui cherche à promouvoir un plan volontaire de soins médicaux payés d'avance. Un tel raisonnement est une menace aux efforts déployés et l'on ne peut dire "cela ne peut survenir ici". D'autre part, quelques-uns de nos gens pensent que malgré nos meilleurs efforts, l'imposition éventuelle de la médecine d'état est inévitable. Cette attitude défaitiste a tendance à faire cesser la lutte pour promouvoir et améliorer nos plans volontaires, et a déjà même fait abandonner la partie chez d'aucuns.

Heureusement, la profession dans son ensemble n'adopte pas l'une ou l'autre de ces attitudes. En suivant la marche des temps et en jouant un rôle important dans le développement et le progrès du Canada, la profession médicale reconnaît le besoin de promouvoir un plan canadien distinctif pour les problèmes de santé qui concernent notre peuple. La profession ne dénie pas la position de l'Etat dans l'organisation des services de santé, et nous croyons qu'elle a démontré son habileté à travailler en harmonie avec les gouvernements à l'avantage de tous les Canadiens.

Le parcours du Président a fourni une excellente occasion pour évaluer la force de notre organisation et de ses divisions. Commençant par la réunion tenue à St-Jean, Terreneuve, notre plus jeune province, il a été évident que les médecins de cette région ont été stimulés et aidés par leur contact avec l'Association Nationale. Dans cette région où les problèmes médicaux sont uniques, la Confédération a eu pour effet d'introduire des services publics tels que la Com-

pensation pour les Travailleurs. La profession considère sa relation avec ce problème et d'autres, une tâche familière à notre organisme partout.

La Division du Nouveau-Brunswick s'est réunie dans un endroit très gai, soit à l'hôtel Algonquin à St-André, et présentait sa soixante-et-onzième session annuelle. La manière facile et efficace de conduire ces assises, témoigne de la longue expérience acquise pour le bien médical de la province et du pays en général.

D'autre part, l'organisation médicale la plus ancienne au Canada, la Division de la Nouvelle-Ecosse, tenait la quatre-vingt-dix-huitième réunion annuelle qui eut lieu à Antigonish. Le local pour ces assises fut mis à notre disposition par l'Université St-François Xavier, et un programme varié fut présenté comprenant des activités techniques, scientifiques et sociales.

La force qui existe dans la Division de l'île du Prince Edouard ne fut jamais autant affirmée qu'à la réunion de cette année à Charlottetown. Les discussions ouvertes au sujet du contrôle du cancer et du programme de la santé mentale, furent des démonstrations persuasives à l'égard du fait que la division occupe une position inté-

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APPLICATION FOR ACCOMMODATION
CANADIAN MEDICAL ASSOCIATION
Banff, Alberta, June 9 to 13, 1952.

Mail this form direct to:

Dr. A. E. Wilson,
904 Greyhound Building,
Calgary, Alberta.

Please make the following reservation for C.M.A. Convention: ☐ Single. ☐ Double. ☐ Twin beds. ☐ Suites.

First choice. Second choice.

at Hotel .....

Cabin .....

Please include names of all persons who will occupy rooms. (PLEASE PRINT).

Name. Address. City. Province or State.

.....

.....

.....

Arriving Banff .....at.....A.M. P.M.....Date of Departure .....

PLEASE RESERVE EARLY:

This application is submitted by me as: ☐ Member of Executive Committee. ☐ Member C.M.A. ☐ Delegate to General Council. ☐ Visiting Doctor. ☐ Contributor to Scientific Program. ☐ Exhibitor.

☐ Member Affiliated Society (Name .....)

Send Confirmation to Doctor .....
(PLEASE PRINT)

....
(City) (Prov. or State)

The following accommodation will be available.

	Single	Double	Twin Beds	Suites
Banff Springs Hotel / Chateau Lake Louise	$16.50 per day	$13.50 per person, per day, two to a room		American Plan

Cabins (limited number) $8.00 to $18.00 per day

Additional accommodation will be available at first class hotels, *i.e.*, King Edward and Mount Royal Hotels at reasonable rates.

Note: DEPLANING POINT FOR BANFF IS CALGARY.

Please Note:

(1) Accommodation at Banff Springs Hotel and Chateau Lake Louise will be considered as one hotel. There will be hourly bus service between Chateau Lake Louise and Banff Springs Hotel.

(2) Single reservations will be assigned to twin bedded rooms for occupancy by two persons, if necessary.

PLEASE CANCEL IMMEDIATELY IF YOUR PLANS CHANGE.

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grante parmi les problèmes immédiats de la province qu'elle représente. Les sessions techniques ont aussi démontré que les médecins de l'île du Prince Edouard sont au courant des problèmes de l'heure.

Au cours des quatre réunions qui ont eu lieu dans les Maritimes, une équipe de conférenciers accompagna le président, et des travaux très efficaces furent présentés au cours des sessions scientifiques. L'Association Médicale Canadienne et ses Divisions remercient ces médecins et professeurs très occupés, de la contribution appréciable qu'ils ont apportée aux études scientifiques qui sont fondamentales dans la poursuite du but de notre organisation. Il est encourageant de remarquer cependant, que les Divisions ne dépendent pas seulement de conférenciers invités pour présenter un programme instructif car les présentations par des conférenciers locaux occupent de plus en plus une place importante dans leur programme.

Le voyage nous amena ensuite dans l'Ouest où la première des quatre réunions nous fit descendre à Moose Jaw où avait lieu la réunion de la Division de la Saskatchewan. Malgré l'ouverture de la chasse aux canards qui avait lieu le même jour, un très grand nombre de médecins et leur épouse s'enregistrèrent. Des activités techniques, scientifiques et sociales se sont poursuivies avec l'enthousiasme caractéristique de nos collègues de Saskatchewan, et à cet endroit, la contribution apportée par des conférenciers locaux au programme scientifique, fut très appréciable.

De là, nous avons assisté à la quarante-sixième réunion annuelle de la Division de l'Alberta à Edmonton. Ici, l'atmosphère stimulante de la capitale des huiles au Canada, et l'influence pondérée de l'Université d'Alberta furent évidentes. Bien que nos collègues d'Alberta soient engagés dans plusiers projets médicaux importants relatifs à leur province, ils ont trouvé le temps de discuter les plans de la quatre-vingt-troisième réunion annuelle de l'Association Médicale Canadienne, qui aura lieu à Banff et au Lac Louise au cours de la semaine de 1952. Le Dr Harold Orr, le président élu et ses comités locaux font actuellement des préparatifs pour un congrès qui sera mémorable.

La Division de la Colombie-Britannique se réunit à Vancouver où une activité variée dura pendant une semaine, y compris l'inauguration de l'Académie de Médecine de Vancouver. Cet édifice moderne offre des lieux très spacieux et abritera la bibliothèque médicale de même que le bureau et les salles de comités pour toutes les organisations médicales de la province. Un tel endroit suscita beaucoup d'envie de la part de tous les visiteurs. Une décision importante se réalisa au cours de cette réunion, et la Division de la Colombie-Britannique a entrepris de financer ses propres activités en demandant une souscription annuelle sur une base volontaire à tous ses membres.

La dernière réunion où assista le Président fut à Winnipeg où eurent lieu les assises de la Division du Manitoba. Ces session bien organisées et avec documents à l'appui, offrirent une conclusion appréciable et instructive à l'égard de cette enquête sur la médecine au Canada d'un littoral à l'autre.

Bien qu'il soit compromettant de tirer des conclusions relatives à la situation qui existe dans un organisme aussi complexe que celui de la profession médicale au Canada, il est possible tout de même d'exprimer l'opinion qui indique que le sujet est actif et vivant, même puissant, et que sous ce rapport, les conditions de la profession médicale marchent de pair avec celle de la nation.

ABSTRACTS *from current literature*

MEDICINE

Anuria in Acute Nephritis.

NABARRO, J. D. N. AND SPENCER, A. G.: BRIT. M. J., 2: 393, 1951.

The composition of body fluids is influenced by cellular metabolism and total intake of fluid, food, and electrolytes in renal homœostasis When there is no effective treatment for renal failure there is an insidious onset of changes in the distribution of body water and electrolytes, progressive acidosis; in the extracellular fluid there is an accumulation of potassium phosphate and urea, by-products of the catabolism of cellular and exogenous proteins. Over-hydration and pulmonary œdema are associated with death from renal failure, and this may be precipitated by the excessive ingestion of fluids or intravenous administration of saline. In temperate climates a 70 kgm. patients needs 1,000 ml. of water to replace extrarenal losses. The dynamic equilibrium of metabolism is upset by fever, starvation, acidosis, dehydration, and secretion of adrenal steroids in excess. Treatment should be to prevent excessive cellular metabolism. All the calories of the diet are derived from the carbohydrate, as protein would increase the potassium intake, increase the total nitrogen metabolism, and increase the acidotic tendency which in turn increases the breakdown of cells and accelerates the transfer of potassium and phosphate into the extracellular fluid. When the plasma potassium is near the dangerous levels peritoneal dialysis or the artificial kidney provide effective means for the removal of excess potassium from the extracellular fluid. When biochemical changes are not too severe dietary control will effectively maintain biochemical homœostasis. This latter method causes the least inconvenience to the patient. Testosterone administration causes protein anabolism and produces a transfer of potassium into the cells from the extracellular fluid in the normal K/N ratio, and it inhibits the output of adrenal steroids, if there is adrenal cortical overactivity in uræmia this would be an additional reason for its use in treatment.

J. A. STEWART DORRANCE

The Natural History of Venous Thrombosis.

RAEBURN, C.: BRIT. M. J., 2: 517, 1951.

The most frequent cause of thrombosis is confining elderly people to bed with or without immobilization of an extremity, and a restriction of abdominal respiration, a venous stasis basis. Platelet adhesiveness does not play as important rôle as was previously thought. Collagen underlying the vascular endothelium and derived from

the fibroblasts tends to undergo an irreversible solgel reaction in impounding blood cells. Biochemical changes in the vascular endothelium permit the permeation of intercollagenous cement substance causing an adhesive tendency and this is the primary vascular defect for the formation of a platelet thrombus. Erythrocytes are retained by the platelets and the thrombus is built up. This is followed by endothelialization and organization. Finally the thrombus becomes a fibrotic nodule containing large capillaries and a few phagocytes laden with pigment. This process continues with the formation of new thrombus at the periphery. In large veins the thrombus may lie free, breaking off segments to cause embolism. J. A. STEWART DORRANCE

Oral Treatment of Polycythæmia Vera with β-Naphthyl-Di-2-Chloroethylamine (R48).

IVERSEN, K. AND MEULENGRACHT, E.: BRIT. M. J., 2: 510, 1951.

The authors report on the treatment of six patients with polycythæmia vera of 3 to 9 years' duration with β-naphthyl-di-2-chloroethylamine or R48, a nitrogen mustard compound, in doses of 300 to 400 mgm. per day. R48 is toxic to the bone marrow and in some cases caused a fall in leucocytes. In two cases there was nausea without vomiting during the first week of oral administration, diarrhœa occurred infrequently and these were the only adverse side effects. In five cases there was a marked remission during the course of treatment lasting from five weeks to two months. The leucocyte values fell to as low as 1,200 per c.mm., a spontaneous and rapid rise commenced in 12 to 14 days after discontinuing the intake of R48. Careful and constant control by blood cytological studies is necessary in the use of R48 as the toxicity to the bone marrow might cause a resultant aplastic anæmia. Five of the six cases studied have had remissions without R48 for 7 to 19 months. The sixth was in remission for 5 months and then was recommenced on R48 therapy because of a rise in hæmoglobin. J. A. STEWART DORRANCE

The Clinical Diagnosis of Dissecting Aneurysm of the Aorta.

BERESFORD, O. D.: BRIT. M. J., 2: 397, 1951.

Dissecting aneurysm of the aorta is seldom made antemortem because of the relative infrequency of the condition, the absence of a characteristic syndrome, the limitations of special diagnostic adjuncts, and almost universal failure to bear the diagnosis in mind. Also detailed examination of the patient is prevented by the extreme illness of the patients. Such a condition is found once in every 400 to 500 necropsies, but this does not include the cases in which the condition has healed. Approximately 80% of cases occur in patients over 50 years of age, and 10% of cases recover. Males predominate over females in a ratio of 65/36, and hypertension occurs in 80% of cases. A radial pulse may be felt in 2.8% of cases, while a femoral pulse may be felt in 7.0% of cases. Other conditions frequently occur in association with aneurysm of the aorta and may mask the true underlying condition, such as coronary occlusion, with decreased or absent peripheral arterial pulsation, or "perforated ulcer" with peripheral sensory loss. Usually the E.C.G. is normal. From the time of onset of symptoms until death is 4 to 7 days and at present the only treatment is adequate sedation. Peripheral vascular disturbances are of great help in the diagnosis of dissecting aneurysm of the aorta and usually occur in more cases than is thought.

J. A. STEWART DORRANCE

SURGERY

Malignant Disease of the Testis.

PROSSER, T. M.: BRIT. J. SURG., 38: 473, 1951.

Biopsy of a tumour of the testis should not be done, rather simple orchidectomy. Removal of the testis is good treatment for most lesions causing tumours, and malignancy can be diagnosed with certainty and less danger of spread. Metastases occur in 54% of teratoma and 35% of seminoma, both spreading to the abdominal lymph nodes and teratoma more frequently to the lungs. All cases should be treated by irradiation after orchidectomy. Of the cases of seminoma treated in this way before clinical evidence of metastases were present, 66% were surviving after five years, of teratoma cases 55% were living after five years. If metastases are present when first seen only 15% were alive after 5 years, but several cases are instanced of nine to fourteen year survivals after repeated irradiation of para-aortic, mediastinal and supraclavicular lymph-node and pulmonary recurrences. Seminomas are often very radio-resistant. Complete surgical dissection of the lymphatic fields is practically impossible. BURNS PLEWES

A Critical Evaluation of Subtotal Gastrectomy for the Cure of Cancer of the Stomach.

MCNEER, G., VANDENBERG, H., SONN, F. Y. AND BOWDEN, L.: ANN. SURG., 134, 2, 1951.

A study of autopsies on patients who had died of recurrence after gastrectomy for carcinoma of the stomach in most of the New York hospitals, showed that 50% had recurrence in the gastric stump, 10% in the duodenal stump and 20% in the perigastric lymph nodes and gastric bed as the only local recurring neoplasm. Most also had distant metastases. All the 92 cases had been operated upon for cure, not palliation. In all, 80% of these autopsies showed a failure to control the neoplasm locally. 14 cases died of metastases with no local malignant growth and 4 died of unrelated cause and showed no evidence of cancer. The average survival rate of those who died of cancer was 20 months. Neither the size of the lesion nor its histologic type influenced the chance of local recurrence. It is concluded that about half of the patients operated upon for carcinoma of the stomach may have been denied the chance for cure because an inadequate amount of stomach, duodenum or lymph nodes were removed. Total gastrectomy is recommended as the most logical operation for carcinoma of the stomach. BURNS PLEWES

Streptokinase and Antibiotics in the Treatment of Clotted Hæmothorax.

CARR, D. AND ROBBINS, S. G.: ANN. SURG., 133: 853, 1951.

Streptococcal fibrobrinolysin and desoxyribonuclease are lysin enzymes and were used in an attempt to prevent the formation of "peel" when a traumatic or postoperative hæmothorax clots or becomes infected. Streptokinase is primarily active against fibrinous exudate while streptodornase is active against the desoxyribose nucleoprotein of empyema. Neither has any lytic effect against organized fibrous tissue. The drugs should not be used in the presence of a bronchopleural fistula.

The use of streptokinase and streptodornase is described in 10 cases. It appears that streptokinase will dissolve fibrin in the pleural cavity promptly and efficiently and that streptodornase is equally effective in rendering purulent exudate thin. Used together they remove substances around colonies of organisms to expose them to injected antibiotics. Decortication may be avoided but their use does not take its place once fibrous organization has occurred. BURNS PLEWES

Chronic Empyema.

SELLORS, T. H. AND CRUICKSHANK, G.: BRIT. J. SURG., 38: 411, 1951.

A full discussion of chronic empyema is based on a study of over 600 non-tuberculous cases. The pathology of pleural infections is illustrated by photomicrographs and pleurograms. The causes of chronic empyema come mostly under the heading of maltreatment of acute empyema: late or wrong drainage, or "penicillin" empyema, but abscess, bronchiectasis, new growth,

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actinomycosis and foreign bodies are also included, as are a group of causes following operations or associated with other diseases such as subphrenic abscess, œsophageal fistula and liver abscess. The authors always operate for empyema with the patient erect or sitting and emphasize that the paravertebral gutter is the commonest site of empyema so that the old teaching that the axillary line is the best site for drainage is responsible for many errors. The constant care, frequent examinations and active physiotherapy necessary are described. The bacteriology and incidence of various complications such as bronchopleural fistula, hæmorrhage, cerebral infection, and empyema necessitatis are covered before treatment is discussed. The purpose of the paper is obvious: to improve the early and adequate treatment of acute empyema. BURNS PLEWES

Small-gut Obstruction Following Combined Excision of the Rectum.

GOLIGHER, J. C., LLOYD-DAVIES, O. V. AND ROBERTSON, C. T.: BRIT. J. SURG., 38: 467, 1951.

Intestinal obstruction after resection of the rectum occurred 37 times in a series of 1,302 cases, and 4 others had symptoms but were relieved by conservative measures. Of these, 13 had adhesions not related to the kind of operation done, 1 had strangulation by a Meckel's diverticulum and 1 had a strangulated hernia through the anterior abdominal wound. Twelve cases obstructed because of adhesions or hernia in relation to the reconstructed pelvic floor. In 10 cases the obstructions were about the colostomy: adhesions, hernia into the colostomy wound, hernia between the leaves of the iliac mesocolon and three strangulated herniæ between the abdominal wall and the colostomy. All lateral space strangulations occurred in the 170 cases in which the colostomy was brought out through the paramedian incision, a more convenient situation in obese patients.

The diagnosis, treatment, mortality and results in these cases are discussed in detail. The overall mortality was 19%, including those cases treated expectantly on the erroneous diagnosis of peritoneal recurrences. Suggestions are made regarding alterations in technique of the primary operation to avoid these complications.

BURNS PLEWES

OBSTETRICS AND GYNÆCOLOGY

Sex Hormones in Experimental Diabetes.

HOUSSAY, B. A.: BRIT. M. J., 2: 505, 1951.

This group of experiments shows that after subtotal pancreatectomy diabetes appears in rats with less frequency in the female than the male. This sexual difference is due to the provocative action of the testes and androgens and a protecting influence of the ovaries and œstrogens. The mechanism of protection is apparently chiefly due to the actions of the ovaries and œstrogens in the stimulation of hypertrophy and hyperplasia of the islets of Langerhans with production of new B-cells at the expense of the centro-acinar cells. It is difficult to say yet how far this action occurs in other species. The author would rather not discuss now whether or not it occurs in man.

The peripheral action of œstrogens upon carbohydrate metabolism is not yet well known. The probability of preventing some forms of experimental diabetes, and even of curing a certain proportion of cases of not too severe diabetes, certainly exists.

It is evidently worth while to continue this line of investigation using prolonged administration of those substances already studied and other new ones, either alone or combined with insulin, in order to prevent or treat other types of experimental diabetes, and eventually human diabetes. It would be of value to discover substances which have no œstrogenic effect but cause hyperplasia of the islets and inhibit the hypophysis or adrenals. Diabetes can possibly be controlled by other mechanisms, such as direct or indirect action on tissue metabolism. Experimental medicine has given us most of our fundamental knowledge of diabetes, and it seems that it will continue to increase this knowledge. It also gives hope that new methods to prevent or even cure this disease may be discovered. ROSS MITCHELL

Pudendal Block with Hyaluronidase.

HEINS, H. C.: AM. J. OBST. AND GYNEC., 62: 658, 1951.

Hyaluronidase is a useful adjunct to the anæsthetic mixture for pudendal block since a much higher percentage of ideal blocks was secured with hyaluronidase (80%) than without this drug added to the solution (28%). There is a very rapid onset of anæsthesia. A much smaller amount of anæsthesic solution is needed for adequate blocks. There were no local or systemic reactions to the hyaluronidase. ROSS MITCHELL

Infectious Hepatitis in Pregnancy.

MICKAL, A.: AM. J. OBST. AND GYNEC., 62: 409, 1951.

Thirteen cases of infections hepatitis without acute yellow atrophy and two cases with acute yellow atrophy associated with pregnancy were seen at Charity Hospital of New Orleans from 1940 through 1949. During this time 69,186 mothers were delivered, making the incidence of the disease 0.022%. There were two deaths, giving a mortality rate of 13.3%. Conservative treatment is the procedure of choice for both the hepatitis and the pregnancy. The nutritional state of the patient is an important factor in the course that the disease will follow. Postpartal hæmorrhage, usually delayed and severe, was encountered in all cases of acute yellow atrophy of the liver.

The infants showed no effect of the maternal disease. Only one infant (premature stillborn) died, 12 survived, giving fetal survival rate of 92.3%.

Labour and delivery were not adversely affected by the hepatitis. Acute yellow atrophy need no longer be considered a separate obstetric entity. ROSS MITCHELL

PÆDIATRICS

Study on Orange Juice, Orange Juice Concentrate, and Orange Peel Oil in Infants and Children.

JOSLIN, C. L. AND BRADLEY, J. E.: J. PEDIAT., 39: 325, 1951.

Vitamin C is necessary for the utilization of acetoamino acids, aiding in the resistance to infections, healing of wounds, collagen formation, and calcium metabolism. The authors studied 406 infants and children from 2 weeks to 6 years of age (14 of whom were eczematous) with regard to regurgitation, bowel movements, skin rashes, skin test sensitivity, the pH of orange juice and orange peel oil, and side effects. Orange peel oil pH averaged 5.65, while the pH of orange juice concentrate averaged 3.76. Patch tests showed that 1.8% of the group studied were sensitive to orange juice, while 5.3% were sensitive to orange peel oil. No disturbances of bowel function could be attributed to the orange juice preparations. Orange juice feedings were commenced at the beginning of the third week, starting with ¼ ounce of orange juice diluted with an equal volume of water and gradually increasing it with the volumes of the other formulæ. The orange juice should be extracted from the fresh fruit with a maximal reduction of peel oil by gentle squeezing rather than by exerting undue pressure on the peel. J. A. STEWART DORRANCE

The Use of Ascorbic Acid Tablets to Enrich Milk for Infant Feedings

HOLMES, A. D., JONES, C. P. AND TRIPPS, F.: J. PEDIAT., 39: 320, 1951.

The reduced ascorbic acid of milk in clear glass bottles is oxidized very rapidly, and none remains after ½ hour of exposure to bright sunshine. The rates of loss of re-

duced ascorbic acid of milk stored in dark refrigerators is from 84.8 mgm./l. on the first day to 55.1 mgm./l. on the fifth day. The diet of an infant may be supplemented by orange juice, but this medium contains a variable amount of reduced ascorbic acid depending on the type of fruit, geographical region of growth, seasonal date of picking, and position on the tree in relation to exposure to sunlight. The authors suggest the use of suitably prepared tablets containing reduced ascorbic acid which might be added to the formula as it is prepared, in order to ensure a standardized uniform amount of reduced ascorbic acid sufficient to meet the daily nutritional requirements of infants.

J. A. STEWART DORRANCE

The Electrocardiogram in the First Two Months of Life.

FURMAN, R. A. AND HALLORAN, W. R.: J. PEDIAT., 39: 307, 1951.

The authors studied 70 electrocardiograms obtained from 52 patients, all of whom had normal chest roentgenograms and negative physical examinations. During this neonatal period there are constant findings in the mechanism, heart rate, P-R interval, QRS duration, duration of electric systole, S-T junction, P and Q waves. The T wave does not show changes during the first few days of life and by the second week it shows a transition to the subsequent normal of this period. During the third week there is a marked decrease in the right ventricular preponderance characteristic shortly after birth.

J. A. STEWART DORRANCE

The Effect of Cortisone on Nutrition.

GEPPERT, L. J., O'HARA, B. F. AND PEAT, A. C.: J. PEDIAT., 39: 267, 1951.

Patients receiving cortisone experience two types of gain in body weight; a progressive nutritional gain, not quickly decreased upon discontinuing cortisone therapy, and a rapid, fluctuating, unstable weight gain due to œdema and retention of fluid, which disappears quickly within a few days when cortisone is discontinued. The authors studied three child patients on cortisone therapy to distinguish between the two types of gain in body weight due to nitrogen retention and fluid retention. In all three cases, while on large initial loading doses of cortisone, there was a marked bulimia and a concomitant rise in caloric, nitrogen, electrolyte, and water intake, this counterbalanced the antianabolic and hypokalæmic effects to maintain normal serum levels. The increased intake of potassium and nitrogen is desired, but the retention of sodium and chloride causing an increase in extracellular fluid and œdema may indicate cessation of therapy. Consequently the diet should contain a minimum of salt and potassium administration is unnecessary if there is an adequate food intake. Appetite was increased four to five-fold in 48 to 72 hours after cortisone therapy was commenced, and the undesirable gain in body weight due to œdema may be prevented by restricting the salt in the diet.

J. A. STEWART DORRANCE

Cerebral Palsy in Children.

BAKWIN, R. M. AND BAKWIN, H.: J. PEDIAT., 39: 113, 1951.

The incidence of cerebral palsy is 7 children born per year per 100,000 population. Etiological factors are varied, frequently the child is the first born of a woman in the fourth decade. There is a high incidence of a maternal history of abortions, premature labours, and stillbirths, complicated by hyperemesis gravidarum, anæmia, and hæmorrhages. Precipitate delivery and other difficulties of delivery are frequent. In 66% of cerebral palsied children there is a neonatal history of cyanosis, twitching, convulsions, crying and vomiting. Injury at birth occurs in 55%, congenital cerebral defects in 23%, and postnatal head injury in 5%. Premature infants with increased fragility of blood vessels and softer cranial bones often show an increased incidence of cerebral palsy. There are five types, spastic 40%, athetoid 40 to 45%, ataxia 10%, tremorous 5% and rigid 5%. One-third of cerebral palsied children are feeble-minded, most often in the spastic and rigid groups. Mental performance may be reduced by the over-use of anti-epileptiform drugs. Special consideration should be given to these handicapped children in school, preferably in separate classes. Speech disturbances occur in 75%, and some cerebral palsied children never acquire speech while many are benefited by speech therapy. Reading may be taught when the child has a mental age of 6 years. The cerebral palsied child's reactions to his disability are: (1) depression; (2) anxiety; (3) resentment; (4) resignation and indifference; (5) defiance. The reaction is determined by the attitude of other people, particularly the parents. During adolescence the handicapped child realizes more than ever that he is not fully equipped to face adult life. The management of a cerebral palsied child should be toward ultimate independence, a well developed social sense, and if possible eventful gainful employment in an occupation he can fulfil without anxiety or frustration.

J. A. STEWART DORRANCE

DERMATOLOGY

Wool As a Cause of Eczema in Children.

HILL, L. W.: NEW ENGLAND J. MED., 245: 407, 1951.

This is a seasonal topic, for as Hill, the widely-known Boston pædiatrician points out, wool is a frequent cause of eczema in children "veritably smothered in wool in winter", which recurs at the onset of cold weather and begins to improve as warm weather returns. The favoured sites are the front of the neck, the ankles, wrists, backs of hands, the arms and the legs. The mother notices that wool produces it. Once started it is aggravated and protracted by the incessant rubbing and scratching, persisting of its own right by reason of the chronic pathologic changes thus produced, irrespective of further contact with the allergen. Absorption of the allergen from the abraded area, possibly also from inhalation of wool dust, probably accounts for its appearance on parts of the body not in contact with wool. Positive scratch tests are uncommon; all positive patch tests are clinically significant; no strongly positive intracutaneous tests were observed in the author's series, and their significance was considered doubtful. The ordinary patch test of 1 or 2 days is unlikely to give a positive test; the patch must be in place for several days, preferably a week, wet undyed wool being used on a lightly abraded area. Hill advises that the local medication be covered by soft white cotton cloth (never gauze), snugly bandaged in place with several layers of 2-inch elastic bandage for 24 hours in the day.

D. E. H. CLEVELAND

Is Mycosis Fungoides a Reticuloendothelial Neoplastic Entity?

CAWLEY, E. P., CURTIS, A. C. AND LEACH, J. E. K.: ARCH. DERM. AND SYPH., 64: 255, 1951.

"Within recent years the pendulum of dermatological opinion has swung away from an infectious cause (for mycosis fungoides) and has placed the disease quite securely among the lymphoblastomas, thus emphasizing its probable neoplastic nature". The disease is ordinarily described as presenting three stages: (1) the premycotic or erythematous, showing red, scaly nondescript lesions often mimicking eczema, psoriasis, seborrhœic dermatitis, erythema multiforme and exfoliative dermatitis; (2) the infiltrative stage showing plaques of bizarre configuration and vivid colour; (3) the fungoid stage consisting of livid red tumours. Intractable pruritus commonly characterizes the first two stages. The insidious onset of the premycotic stage may occasion much diagnostic confusion and a period of observation is often necessary before diagnosis can be established. The disease is one of later life and there is a male sex-pre-

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dominance. Of the 10 cases reviewed in detail by the authors, in the University of Michigan Hospital, cutaneous lesions had been present at the time of admission for periods varying from 6 months to 43 years. Repeated and careful examination failed to show a typical blood picture associated with the disease. Significant roentgenological findings were of no help in establishing the diagnosis; no osseous changes of the disease have been demonstrated. In 8 of the 10 patients involvement of structures and organs other than the skin occurred, and the disease must no longer be regarded as a strictly dermatological disorder. There was a remarkable variation found in the microscopic studies of involved tissue. These are given and illustrated in much detail, and in the 10 cases of "unequivocal clinical examples of mycosis fungoides . . . the pathological findings . . . clearly uphold the alleged reticuloendothelial origin of mycosis fungoides and its classification among the lymphoblastomas but militate against its recognition as a pathological entity." Death resulted in 5 cases from cachexia, in 4 from lymphoblastomatous involvement of structures and organs other than skin, and intercurrent infection in 1. D. E. H. CLEVELAND

The Cutaneous Toxicity and Therapeutic Effectiveness of Penicillin O.

MARSH, R. R. AND TILLOTSON, J. G.: NEW ENGLAND J. MED., 245: 17, 1951.

Penicillin G has a high sensitizing index, which in the opinion of many precludes its use as a topical remedy, and demands caution even in its parenteral use. Many different penicillins have been produced by altering the composition of the culture media, and one, because of its antibiotic potency, and its rare production of reactions, called Penicillin O because of its onion-like odour, has been studied and is reported on. 50 of 52 hospitalized patients were treated with penicillin O by intramuscular injection, and two by aerosol inhalation. One patient was given intrathecal injections in addition to intramuscular. In 4 patients cutaneous reactions occurred; 2 of these were in a group of 5 known to have reacted previously to penicillin, and 2 occurred in 4 patients definitely known to have had no previous injections of penicillin. The eruptions resulting in the 4 cases were pruritic macular or maculo-papular rashes, in one case accompanied by facial œdema. The eruptions subsided in a few days after withdrawal. *In vitro* studies have shown that penicillin O has essentially the same antibiotic activity as penicillin G, and in some cases at least will not cause reactions in patients who have previously developed toxic eruptions from the latter drug. D. E. H. CLEVELAND

Dermatitis from Local Anæsthetics. With a Review of 107 Cases from the Literature.

LANE, C. G. AND LUIKART II, R.: J. A. M. A., 146: 717, 1951.

The condition described is one, which as the authors state is not uncommon, and has not lost in news value since the report by Mook in 1920. Procaine dermatitis among dentists is a matter of common knowledge. Cases are encountered more commonly than the paucity of literature would suggest, among users of ointments and creams containing local anæsthetics, especially when used to relieve pruritus, and particularly in the presence of an already irritated skin. Amongst the commoner of these are butesin picrate, pontocaine, nupercaine, benzocaine and butyn. There is a very wide use of the local application of anæsthetic agents, many firms having produced preparations for relief of cutaneous symptoms in much the same way as the antihistaminic preparations are being brought out today. The authors consider that it would be advisable that some sort of warning concerning possible sensitization should accompany such preparations when prescribed for local use. In the discussion following presentation of the report it was stated that a fundamental error has been made in assuming that a substance which will anæsthetize the conjunctiva or produces anæsthesia on injection will relieve itching on application to unbroken skin. Research so far has not found this to be the case. D. E. H. CLEVELAND

Electron Microscope Study of Epidermal Fibres.

ADOLPH, W. E., BAKER, R. E. AND LEIBY, G. M.: SCIENCE, 113: 658, 1951.

Various explanations have been given of the intracellular fibres in the stratum spinulosum of the epidermis, which have been put forward over many years. One of the most widely accepted has been that they are extensions of the intercellular bridges, but others have regarded them as artifacts. The above workers in the School of Medicine of the University of Southern California examining sections cut at right angles to the skin surface with the electron microscope have shown that the intercellular bridges appear to terminate at the cell boundaries, but cannot decide whether they are protoplasmic or not. They show that a fine feltwork of fibres are present in the precipitated cytoplasm of the cells, but they are of a different order of size than the intercellular fibres and are laid down in a random manner having no apparent relation to them. They believe that they are most probably an impression of intracellular fibres lying just above or below the plane of focus of the light microscope and are thus artefactal due to the limited depth of field of the instrument. D. E. H. CLEVELAND

PSYCHIATRY

Value of Antabuse as Adjunct Therapy for Alcoholism.

WEXBERG, L. E. *et al.*: MED. ANN., DISTRICT COLUMBIA, 20: 202, 1951.

Wexberg and associates discuss the use of antabuse (tetraethylthiuram disulphide) as an adjunct in the rehabilitation of alcoholics and stress that the patient must have at least average intelligence and must realize the risk he incurs should he return to drinking alcohol while taking antabuse. The patient's intelligence and motivation should be ascertained by psychological tests (*e.g.*, Rorschach and thematic apperception tests). Psychiatric inquiry should also be used. This covers the patient's early history, social adaptability, educational level, work status, marital relations, religious background, and the development of the drinking problem. A complete physical survey is also needed and should include electroencephalogram, electrocardiogram, test of basal metabolic rate, liver and kidney function studies, and a glucose tolerance test. Contraindications to the use of antabuse are diabetes mellitus, cirrhosis of the liver, chronic or acute nephritis, myocardial failure, coronary sclerosis, pregnancy, epilepsy, and exophthalmic goitre. The patient must not drink for four or five days before antabuse is given. The first dose of the drug is 2 gm. This is decreased by half a gram each day to the maintenance dose of about 0.75 gm. The drug is given daily before breakfast. On the eighth day of treatment the patient is given 15 c.c. of 90-proof whiskey every 15 min. After about three doses a reaction follows, the peak of which is reached in 30 to 60 min. The first and second tests with alcohol should be made in a hospital. Should the antabuse-alcohol reaction be too severe, 1,000 c.c. of 5% glucose in isotonic sodium chloride solution with 1,000 mgm. of ascorbic acid should be given intravenously. Ephedrine, 24 mgm., should be given intravenously if the blood pressure drops alarmingly. So that possible insidious toxic effects of the drug may be discovered, complete blood cell count, liver function studies, basal metabolic rate determination, and urinalysis should be done at frequent intervals. F. W. HANLEY

INDUSTRIAL MEDICINE

The Specialist Looks at Everyday Medical Care in Industry: Psychiatry.

DUE, F. O.: J. A. M. A., 146: 1183, 1951.

Many lost hours in terms of manpower could be saved by the consideration that employees are persons who

react to even subtle stresses and tensions. The doctor has special confidence from the worker and his attitudes can be very influential. The chief emphasis must be placed in prevention of disability from emotional disturbances and psychiatric illnesses that could arise from complications in the worker's industrial and personal life.

Perhaps the greatest step toward the development of a psychiatric orientation in the medical staff is the cultivation of an alert awareness of the emotional attitudes and tensions in the everyday lives of the workers to which care is administered. A disciplinary, judgmental and critical attitude should be avoided. Physicians and nurses should be able to produce in the patient the feeling that they are friendly and impartial confidants who will at all times try to see the patient's side of the story. Even if the patient's complaints do not seem valid or concrete, the interviewer should consider that every complaint represents some real problem for the complainant. It is the physician's task to try to diagnose the latent problem. Besides careful history taking, the patient's manner of relating his history and complaints, an evaluation of his facial expressions and the amount of pressure apparent in his general speech and attitudes, should all be recorded as possible signs of emotional factors in the presenting complaints. Treatment that can be given by the industrial medical team may include permissive listening to the patient, recommendations, reassurances, suggestions, and manipulation of the environment. Certain symptoms afford clues in themselves to the exciting agent, *e.g.*, recurrent headaches often indicate underlying resentment that cannot be expressed. Referrals of more serious conditions should be prepared carefully for referral to a psychiatrist, the patient being told frankly the type of specialist he is being sent to.

Special psychiatric problems, *e.g.*, alcoholism, accident-proneness and compensation are discussed. With regard to the last, the author points out that many patients claiming compensation are bandied about until they become confused and resentful, and by the time they reach a psychiatrist it is impossible to resolve the complicated superstructure of grievances and countergrievances without complete settlement of the case by cash payment. He believes that many compensation cases that terminate in court battles do so through continued episodes of mismanagement. Many such outcomes can be avoided by careful investigation of the emotional factors at the time the injury is sustained, along with sympathetic and understanding management early in the condition.

F. W. HANLEY

The Epidemiology and Social Significance of Atmospheric Smoke Pollution.

McDONALD, J. C., DRINKER, P. AND GORDON, J. E.: AM. J. M. SC., 221: 325, 1951.

In its relation to public health, the purity of the air we breathe is significant. Smoke pollution of the atmosphere is an old problem. For at least a century investigators have tried to evaluate its alleged detrimental effects on climate, health, animals, vegetation, buildings and other structures, but only rarely have their results been pooled and the total cost of smoke assessed. In this article the authors review what is known about atmospheric pollution due to smoke, as it occurs in urban communities. They deal only indirectly with the many contaminants other than smoke which are introduced into the air in the course of industrial processes. Information on this subject is presented with considerable detail, under the following headings: the epidemiologic problems, smoke as an agent of disease, environmental determinants of smoke, smoke and man's environment, smoke and human health, and, experimental studies. Using the existing evidence the authors then attempt to evaluate the direct influence of atmospheric smoke pollution on human health.

That the dosage of the agent at work in any community is determined by the nature and quantity of fuel, the methods of combustion, the topography, and the meteorological factors, is certain. The case against smoke stands or falls by its effect on the respiratory tract. So far there is no way of separating the influence of a period of high concentration of smoke from the influence of the environment which determines that concentration. The authors emphasize that multiple causation is the rule in natural disease. Smoke itself is a mixture of many potential agents and it seems reasonable to expect some degree of synergistic action both between them and between infective and climatic factors. In their opinion its carcinogenic activity must be left as an open question. Further investigation along that line is justified. The need for further evaluation of smoke as an agent of disease, is clear. The authors suggest the following lines of investigation: (1) The best possible use of available data. Past efforts have been inconclusive. (2) Laboratory studies on animals to assess synergism and antagonism among components of smoke, infective agents, temperature and relative humidity, in their action upon respiratory tissue. (3) Field studies of specific population groups to yield information on the range of variation of susceptibility of human beings to the effect of certain irritants and of factors which influence it.

MARGARET H. WILTON

Heart Disease and Industrial Medicine . . . Recent Trends in the Evaluation of the Cardiac Worker.

HYMAN, A. S.: NEW YORK STATE J. MED., 50: 1603, 1950.

In this article the author presents the dual rôle to be played by industrial medicine in the consideration of the worker handicapped by potential or actual cardiovascular disease. Of major importance as far as management is concerned, is the detection of the candidate for coronary disability before the episode occurs. The worker with an impaired coronary mechanism must not be permitted to attempt physical strain beyond toleration limits. The man who has heart disease must receive consideration. Industrial medicine must find a place in the scheme of occupational self-sufficiency for such employees; their various skills and experience constitute a rich supply of manpower which has been neglected.

The cardiovascular diseases have played an increasingly important rôle during the last one or two decades. For many years the causal relationship between trauma or physical strain and the development of cardiovascular disability has been the subject of much medical and legal controversy. The "reasonable time" between the provocative stress and the development of the acute heart attack, has been interpreted in different ways. Animal experimental work suggests that physical exhaustion alone is insufficient to produce heart disease. The causal relationship is indicated when symptoms of the cardiac episode follow promptly after the performance of the exhaustion phenomenon.

In 1940 a special committee of the New York Cardiological Society was set up to study this problem. Careful investigation of case records from a number of the larger hospitals in New York City indicated that in industrial medicine there is a very close association between unusual or prolonged muscular work and the onset of the clinical syndrome diagnosed as acute coronary thrombosis and occlusion. In about 70% of the cases, the episode occurred within six hours after the alleged stress had taken place; 44% developed coronary occlusion within an hour. Of particular importance was the discovery that in nearly every instance there was a presumptive or actual history of pre-existing coronary insufficiency. In consideration of this fact, the need for pre-employment physical and psychiatric examination is obvious. A simple physical examination will reveal the potential cardiac patient; high blood pressure, murmurs, tachycardia, irregularities and abnormal electrocardiograms will immediately screen out the candidates most likely to become an industrial medical casualty. Brief consideration is given of the syndrome "coronary insufficiency" and also of the use of exercise tolerance tests for the determination of coronary capacity for work. Reference is made also to a few health hazards in industry capable of causing disease

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to the normal heart *per se*. The rehabilitation of the so-called "cardiac cripple" is considered. The data from a number of surveys indicate that where a job can be fitted to the physical limitation of the specific heart condition, the employee has a better than average service record. With continued medical supervision many such individuals with cardiac disabilities have been able to carry on their ordinary life expectancy.

In the author's opinion industrial medicine should emphasize its rehabilitation programs to the end that cardiac cripples as well as all others with physical disabilities may have an opportunity to share in the country's productive capacity. MARGARET H. WILTON

FORTHCOMING MEETINGS

CANADA

CANADIAN PUBLIC HEALTH ASSOCIATION, Christmas Meeting of the Laboratory Section, Royal York Hotel, Toronto, Ont., December 17-18, 1951.

CANADIAN ASSOCIATION OF RADIOLOGISTS, First Mid-Winter Annual Meeting, Winnipeg, Manitoba, January 16-18, 1952.

CANADIAN MEDICAL ASSOCIATION, Banff, Alberta, June 9-13, 1952.

UNITED STATES

THE RADIOLOGICAL SOCIETY OF NORTH AMERICA, 37th Annual Meeting, Palmer House, Chicago, Ill., December 2-7, 1951.

AMERICAN MEDICAL ASSOCIATION, Clinical Session, Los Angeles, Cal., December 4-7, 1951.

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY, Dallas, Texas, May 8-10, 1952.

AMERICAN MEDICAL ASSOCIATION, Annual Session, Chicago, Ill., June 9-13, 1952.

OTHER COUNTRIES

PAN-AMERICAN CONGRESS OF PÆDIATRICS, Montevideo, Uruguay, December 5-8, 1951.

WORLD FEDERATION FOR MENTAL HEALTH, Mexico City, Mexico, December 6-12, 1951.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, Mexico City, Mexico, December 11-19, 1951.

PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY, Fourth Congress, Mexico City, Mexico, January 6-12, 1952.

COLSTON RESEARCH SOCIETY AND UNIVERSITY OF BRISTOL, Symposium on the Supra-renal Cortex, Bristol, Eng., March 31 to April 4, 1952.

COMMONWEALTH AND EMPIRE HEALTH AND TUBERCULOSIS CONFERENCE, Third Conference, Central Hall, London, England, July 8-13, 1952.

BRITISH CONGRESS OF OBSTETRICS AND GYNÆCOLOGY, Thirteenth Congress, Leeds, Yorkshire, England, July 8-11, 1952.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, London, England, July 14-19, 1952.

INTERNATIONAL CONGRESS OF DERMATOLOGY, Fourth Congress, London, England, July 21-26, 1952.

NEWS ITEMS

ALBERTA

Dr. R. M. Parsons of Red Deer is making a speedy recovery following an operation at the University Hospital. Dr. Parsons is a Past-President of the Canadian Medical Association, Alberta Division. We wish him continued good health.

We are sorry to relate the loss sustained by Dr. and Mrs. Frank Law of Edmonton in the accident of recent date in which their son lost his life. The sympathy of the profession is extended to them.

Dr. Morley Tuttle of Calgary and Dr. G. S. Gray of Lethbridge have been appointed Associate Editors of the *Alberta Medical Bulletin*. This quarterly medical magazine for the Province of Alberta has been growing in importance through the continual co-operation of the authors who have put their thoughts into words regarding the varying aspects of medical practice.

Dr. James O. Metcalf has returned to Edmonton following completion of his training in genito-urinary surgery in Kingston and Toronto. Dr. Metcalf completes his five years' training and is now associated with Dr. Gordon N. Ellis. Dr. Metcalf served with the R.C.A.M.C. in the last war, he is a graduate of the University of Alberta.

During the recent visit of their Highnesses, Princess Elizabeth and Prince Philip to Edmonton a stop was made at the Col. Mewburn Hospital where many an old soldier and younger ones had an opportunity to meet their future Queen and her Consort, Prince Philip. Dr. F. G. Ramsay and Dr. A. C. McGugan welcomed and accompanied the Royal Guests through the hospital.

Dr. W. B. Leach, Director of the Pathological Department of the Royal Alexandra Hospital in Edmonton has received Certification in his Specialty from the Royal College of P. & S.[C.]. Dr. Leach is a graduate of the University of Manitoba. He served with the R.C.A.M.C.

Dr. L. A. Rook, M.A., M.R.C.S., D.O.M.S. has recently joined the medical staff of the Medical Arts Clinic in Lethbridge.

Dr. Douglas S. Gorrell of Calgary has been elected a Member of the Broncho-œsophageal Association of America. Dr. Gorrell is also certified in his specialty of Ophthalmology R.C.P.S.[C.], and R.O.L. by the Senate of the University of Alberta.

Dr. Dorothy Barnhouse of Edmonton has returned from a postgraduate tour of England, Sweden, Denmark and France. Dr. Barnhouse is on the Anæsthesiology Department of the University Hospital. During the war Dr. Barnhouse served with the R.A.M.C. in Africa and on the Continent.

Dr. Colin A. Ross, a graduate of the University of Alberta, has returned to Edmonton following the completion of his training in Thoracic Surgery in Newcastle-upon-Tyne under Mr. George Mason, F.R.C.S., for two and a half years. This was followed by a tour of Oslo, Stockholm and the Continent. W. C. WHITESIDE

BRITISH COLUMBIA

The Annual Meeting of the British Columbia Division of the Canadian Medical Association, held on October 3 to 5, was a very successful one. It marked the inauguration of the new Division, which takes the place of the old British Columbia Medical Association. It met under the presidency of Dr. H. A. Mooney, of Courtney,

B.C. The President of the Canadian Medical Association, Dr. H. B. Church, and Dr. A. Kelly, Assistant General Secretary, were welcome visitors at the meeting.

The Annual Meeting of the British Columbia College of Physicians and Surgeons was held on Monday, October 1, in the Hotel Vancouver, under the presidency of Dr. A. B. Nash, President of the Council. It was interrupted in the afternoon by the opening of the new Academy of Medicine, on Burrard Street at Tenth Avenue. The building was opened officially by the Honourable A. D. Turnbull, Minister of Health in the B.C. Government. A large crowd of visitors and guests was present, and took the opportunity to inspect the new building, and the magnificent Library of the Vancouver Medical Association. Tea was served in the large lounge on the lower floor.

The scientific program of the B.C. Division of the Canadian Medical Association was an excellent one. The addresses were all of a very high order, and attracted large audiences. Clinics and Round Table Discussions rounded out the program.

The entertainment programs, for both men and women, was also very well organized and carried out. Golf, water trips, a buffet supper, dance and a final dinner were among the attractions. The highlight of the dinner, at which medical men and their ladies were present, was an address by Dr. William Boyd, Professor of Pathology, at the University of British Columbia. Dr. Boyd is one of Canadian medicine's finest speakers—and one says this most deliberately and sincerely. The manner of his speeches, no less than the matter, is full of charm and makes a speech from him a delight to hear. The University of British Columbia is indeed fortunate in having as its Professor of Pathology, a man of the international reputation and wide scholarship of Dr. Boyd.

Other outstanding appointments to the Faculty of Medicine in the University of British Columbia are those of Dr. John E. McCreary to the chair of pædiatrics, and Dr. James G. Foulks to that of pharmacology. Dr. McCreary comes from Toronto, where he was attending physician at the Hospital for Sick Children for several years—and is a recognized authority on pædiatrics. Dr. Foulks is a graduate of Johns Hopkins and Columbia Universities, and is well known as an expert on diseases of the kidney.

The British Columbia Hospital Insurance Scheme is still the centre of a great deal of discussion in political circles. The Commission of Enquiry appointed by the Legislature in its last session, and headed by Mr. Sydney Smith, M.L.A., has concluded its tremendous task of visiting every hospital centre in British Columbia, and hearing representations from hospital authorities, doctors, administrators, and everyone who had anything they wished to say to them. The Commission then visited Saskatchewan, to enquire into the workings of the hospital insurance plans operating there. They have done, without doubt, a tremendous job, and in a very short time. Those of us who met them were impressed by their intense earnestness, and their terrier-like determination to get down to the very bottom of everything. There was never the slightest hint of partisanship or political manœuvering: all the members, of every party, worked harmoniously together, and with only one object in view, to get all the facts.

The writing of their Report will take some months, but an interim report has been given, and Premier Byron Johnson has assured the Committee that it will get the fullest co-operation from the Government.

Out of it all there would seem to emerge one thing—that everyone in the Province wants to see Hospital Insurance continue, and there is a general feeling that when the various inequalities and administrative difficulties are ironed out, a generally satisfactory scheme will emerge. But it is more than probable that there will still be some fireworks before everyone has had his say in the final disposition of the problem.

J. H. MACDERMOT

MANITOBA

Dr. Morley R. Elliott has been appointed deputy minister of health and public welfare effective September 1. He succeeds Dr. F. W. Jackson who left in October, 1948, to accept a position with the federal ministry of health. In the interim Dr. C. R. Lonovan was acting deputy minister but ill health has obliged him to take extended leave. Dr. Elliott has been on the permanent staff of the provincial health department since 1937 but had a distinguished war record from 1939 to 1945. In May, 1951, he was named president of the Canadian Public Health Association.

Dr. and Mrs. Charles H. Read with their two children have arrived in Winnipeg. Born at Amherst, N.S., Dr. Read received the B.Sc. degree from Acadia University and the M.D.C.M. degree from McGill. He will act as assistant to Dr. H. Bruce Chown professor of Pædiatrics.

Dr. and Mrs. W. H. T. Peake of Transcona recently celebrated their fiftieth wedding anniversary.

ROSS MITCHELL

NEW BRUNSWICK

Dr. L. J. Stephen of East Saint John has been appointed to the Out Patient Medical Service at the Saint John General Hospital.

Dr. D. R. Howell of Dalhousie Medical School appeared by invitation at the September meeting of the Saint John Medical Society. Dr. Howell discussed skin infections with particular reference to conditions seen in general practice and outlined treatments which he has found helpful.

Dr. M. I. Polowin and Dr. S. M. Tobin have received appointments to the associate staff of the Saint John General Hospital.

As part of the postgraduate program of extramural lectures of Dalhousie University, Dr. Martin H. Hoffman, Research Professor of Medicine at Dalhousie, appeared at Campbellton October 22, at Chatham October 23, Moncton October 24 and at Charlottetown October 25. His addresses included (1) Basic principles of the diagnosis and management of Diabetes Mellitus. (2) Use of Hormones in General Practice. (3) Medical Aspects of Thyroid Disease.

In New Brunswick a diabetes detection drive in Diabetes Week is under the direction of Dr. R. E. Washburn of Saint John. This drive is an effort to find unsuspected cases of diabetes and to direct such cases to their own physicians for care.

Dr. Beverly L. Jewett of Fredericton is taking postgraduate training in surgery at the Montreal General Hospital.

Dr. Euclide Rioux of Grand Falls has been granted a federal bursary to cover one year's postgraduate study at Toronto University in Public Health.

Dr. R. T. Hayes of Saint John attended the meeting of the American Academy of Ophthalmology and Otolaryngology at Chicago.

The Saint John General Hospital has appointed Dr. J. Alastair Caskey, M.B., Ch.B., from Edinburgh as radiation therapist. Dr. Caskey holds the diploma in Medical Radiotherapy from University of Edinburgh and was lately consultant Radiotherapist on Professor R. Mc-

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Whirter's staff Edinburgh Royal Infirmary; consultant Radiotherapist Scottish Northern Hospital Board and Consultant Radiotherapist Dumfries Royal Infirmary.

Dr. F. W. Stevenson of Saint John is at present confined to the Saint John General Hospital, due to a complaint common to physicians, ulcer.

Dr. C. W. Kelly, superintendant of the Jordan Memorial Sanatorium, welcomed a large group of physicians interested in diagnosis and treatment of tuberculosis to a one day clinical meeting on Oct. 26, at Riverglade, N.B. The program was arranged by the division of tuberculosis control of the N.B. Department of Health. Dr. G. E. Maddison presided. Speakers included Dr. C. W. Kelly, Dr. H. Cranz of Notre Dame de Lourdes Hospital, Dr. Irene Allen of the Saint John Tuberculosis Hospital, Dr. E. W. Ewart of Moncton Tuberculosis Hospital, and Miss Kathleen M. Jackson of the P.E.I. Health Department.

A. S. KIRKLAND

NOVA SCOTIA

Dalhousie medical students benefit by the new scholarship bequest of $72,000 to be used in medicine and the sciences as a memorial to the son of Dr. and Mrs. James Ross Smith who died during his student days at Dalhousie. The grant was made in the will of the late Mrs. Smith.

Grants by the Federal and Provincial governments of $200,000 each to St. Rita's Hospital in Sydney have been announced. This makes secure the financial venture in the construction of the new 170 bed hospital which is already well underway.

The Halifax Medical Society reversed the decision of its executive in limiting its meetings through the current year to the special monthly sessions called for the purpose of hearing guest speakers. Despite the realization that meetings are coming to take almost as great a portion of the medical man's time as the filling in of health insurance forms, the Halifax profession felt that the monthly clinical meetings in the hospitals through the city were too important to be thrust aside no matter how worthy the reason, and voted unanimously for their reinstatement.

Dr. J. Sinclair Robertson (Dal. '34) has been appointed Deputy Minister of Health and Deputy Registrar General for Nova Scotia. Dr. George Graham (Dal. '38) succeeds Dr. Robertson as Assistant Deputy Minister of Health.

St. Martha's Hospital, Antigonish, opened its three new wings to the public making even better and broader in scope the distinguished service this hospital has been giving to the people of western Nova Scotia.

Dr. R. B. Cattell of the Lahey Clinic, Boston, visited Halifax speaking there to the profession of the province and giving clinics at the Victoria General Hospital. Dr. Cattell's subjects were: Cancer of the Large Bowel and Surgery of the Pancreas and the Biliary System. He appeared under auspices of the Dalhousie Postgraduate Committee.

Dr. G. Ronald Forbes of Kentville has been made a Fellow of the American College of Cardiology.

Among the speakers at the Royal College of Physicians and Surgeons annual meeting at Quebec were Dr. Martin Hoffman, Dr. Lea Steeves and Dr. W. R. Carl Tupper of Halifax.

Dalhousie's first year medical students attended their first social function in the form of a reception at Shirreff Hall where they met their new faculty on a fraternal basis.

ARTHUR L. MURPHY

ONTARIO

The Medical Alumni of the Hospital for Sick Children presented Dr. Alan Brown with his portrait in oils by Cleeve Horne. Dr. Brown, in turn, presented it to the Hospital. At its unveiling Sir James Spence of Newcastle-on-Tyne spoke on "Children's Hospitals, Past, Present and Future".

The American Academy of Pædiatrics held its annual meeting in Toronto. About 2,300 members registered, 1,000 of these were accompanied by their wives.

The Toronto Diabetes Association held a round table discussion on Dietary Control in Diabetes in October. Dr. George Guest, Cincinnati, Ohio, Dr. Priscilla White, Boston and Dr. Waldo E. Nelson, professor of pædiatrics, Temple University School of Medicine, Philadelphia, took part in the discussion.

Dr. Gordon Murray, Toronto, accompanied by his wife and daughter spent three months in the Antipodes. For five weeks he took over wards in the Royal Prince Alfred Hospital, Sydney. He did general surgery, also cardiovascular surgery and gave postgraduate instruction. At the Royal Australasian College of Surgeons and the Australasian Medical Association lectures were given to undergraduates and to graduates. Lectures were given in Melbourne and Brisbane. On week-ends sheep stations and cattle stations were visited. In Auckland, New Zealand cardiovascular operations were performed. Lectures were given to the Australasian College of Surgeons and to the Medical Association of New Zealand. Lectures were also given in Wellington.

The Department of Ophthalmology in the University of Toronto has started a glaucoma laboratory in the Banting Institute under the direction of Dr. T. H. Hodgson. This has been made possible through a grant from the Ontario Provincial Department of Health through funds provided by federal grant. The laboratory will undertake basic glaucoma studies in conjunction with the glaucoma clinic service. The staff members include Dr. W. P. Callahan, Dr. R. K. MacDonald and Miss S. Henninghausen, technician.

Dr. Andrew Lawrence Chute has been appointed professor of pædiatrics and head of the department at the University of Toronto and physician in chief of the department of pædiatrics at the Hospital for Sick Children. Dr. Chute replaces Dr. Alan Brown who has resigned and who will devote his time to his private practice. Dr. Brown will continue his association with the hospital as an active cosultant. He has been appointed professor emeritus at the university.

Dr. Chute was born in India, where his parents were missionaries, his mother was a physician. He is an Arts graduate of Toronto, he took his M.A. in physiology in 1932, and his M.D. in 1935, winning the Faculty Silver Medal. He interned at the Toronto General Hospital and at the Hospital for Sick Children. The years 1937 to 1939 he spent in London when he was granted his Ph.D. from London University. On his return from London he was appointed to the staff of the Hospital for Sick Children and also as research assistant in the Banting and Best Department of Medical Research.

In July 1940 he joined the Canadian Army, later was attached to the British 8th Army in the desert where he worked for the Department of Army Research for the War Office. After convalescing from a desert wound he returned to the R.C.A.M.C. where he was in charge of a special field research unit. He was with the Canadian Army in Italy and later in Northwest Europe.

After his return to Canada in 1945 he went to the

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New England Deaconess Hospital, Boston, where he did clinical work in diabetes until 1946. He then resumed his appointment as a physician to the Hospital for Sick Children and was appointed an honorary associate professor in the Banting and Best Department of Medical Research. Since the death of Dr. Tisdall he has been associate director of the clinical laboratories in the Hospital for Sick Children. He was admitted to the fellowship in the Royal College of Physicians of Canada in 1948. He is president of the Toronto Diabetes Association and chairman of the medical advisory council of the diabetic Association of Ontario. His wife is a graduate in medicine from the University of Alberta.

The Medical Alumni Association of the University of Toronto held a two-day refresher course at Sunnybrook Hospital in October. At the annual business meeting the medical alumnæ were welcomed. From now on the graduates are not divided according to sex but are all part of one organization. The aim of the association is to promote postgraduate education, to raise funds for scholarships, bursaries and research and to encourage closer relationships between students, faculty and graduates.

The Ontario Association of Pathologists has approved a plan of the Attorney-General's medico-legal division to establish a network of laboratories through the province for making tests in medico-legal cases.

Dr. Henry Graham, professor of infant health at the University of Glasgow, and a brother of the late Dr. Roscoe Graham, delivered the second Vera Moberly Memorial lecture under the sponsorship of the University of Toronto. Vera Moberly was matron of the infants home and the person responsible for the introduction of foster care homes in Toronto. Dr. Graham said that the infant death rate has become the best expression of social services in the community. Deaths in the first month make up a large percentage of deaths in the first year. In most of these cases prematurity is a factor. The incidence of prematurity is affected by the social class of the parents. Infant deaths in the labouring class outnumber, four to one, deaths in the professional class. The need, as he sees it, is for a greater number of trained health visitors who can take the infant and health education into the homes.

The pathology museum of the University of Toronto will in future be known as the William Boyd Museum in honour of Professor Boyd, now of University of British Columbia formerly head of the Department of Pathology and Bacteriology for thirteen years at Toronto.

Dr. S. T. Bobra has been appointed lecturer in the Department of Bacteriology, University of Ottawa.

LILLIAN A. CHASE

QUEBEC

Dr. R. H. E. Elder, Montreal, has been appointed by the Civil Service Commission to the staff of the Department of National Health and Welfare's Laboratory of Hygiene. Under the direction of James Gibbard, chief of the laboratory, Dr. Elder will conduct clinical and laboratory investigations of mycotic diseases and work with hospitals and health departments on methods of establishing good clinical bacteriological services. Dr. Elder was born and educated in Tillsonburg, Ont., and graduated in medicine from the University of Western Ontario, London, in 1949. He interned at Victoria Hospital, London, and for the past year has been lecturer in clinical bacteriology at McGill University, Montreal.

NEWS OF THE MEDICAL SERVICES

Canadian Armed Forces

The following physicians were recently appointed to commissions in the Canadian Army Active Force: Captain F. Malcolm, United Kingdom; Captain J. H. Sherrey, United Kingdom; Captain M. L. Trewin, Kingston, Ontario.

Brigadier W. L. Coke, O.B.E., C.D., R.C.A.M.C., Director General of Medical Services of the Canadian Army visited Prairie and Western Commands during the month of October, inspecting the Active and Reserve Force Army Medical Units in Manitoba, Saskatchewan, Alberta and British Columbia.

The Medical Directors of the Canadian Armed Forces were represented by Surgeon Commander W. J. Elliot, Assistant Medical Director, Royal Canadian Navy, Colonel K. A. Hunter, O.B.E., C.D., Deputy Director General of Medical Services, Canadian Army and Group Captain A. A. G. Corbet, Director of Medical Services, Royal Canadian Air Force, at a meeting of The Association of Military Surgeons of the U.S.A. held in Chicago, October 8 to 10, 1951.

Colonel J. N. B. Crawford, M.B.E., E.D., R.C.A.M.C., senior consultant to the Director General of Medical Services (Army), attended the meeting of the Royal College of Physicians and Surgeons of Canada, held in Quebec City, September 27 and 28, 1951. Colonel Crawford has been honoured by selection as physician in attendance to their Royal Highnesses, The Princess Elizabeth and The Duke of Edinburgh, during the period of their Canadian tour.

Lieut.-Colonel J. S. McCannel, O.B.E., R.C.A.M.C., plans and training officer of the Director General of Medical Services Directorate, visited the U.K. and Western Europe in the early part of October, 1951, to make preliminary medical arrangements for the reception of the 27 Canadian Infantry Brigade.

The status of the R.C.A.F. Institute of Aviation Medicine, 1107 Avenue Road, Toronto, has now been raised to that of a self-contained unit. Group Captain B. C. Coles is the Commanding Officer. Dr. Coles has extensive experience in research during World War II.

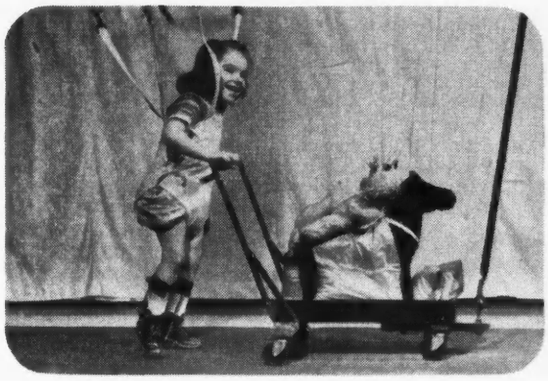
The graduation ceremony for the first para-rescue course held entirely for medical personnel was held October 26, 1951, at R.C.A.F. Station, Edmonton. Air Marshall W. A. Curtis, C.B., C.B.E., D.S.C., E.D., LL.D., Chief of the Air Staff, presented the badges to the graduates and addressed the members of the course.

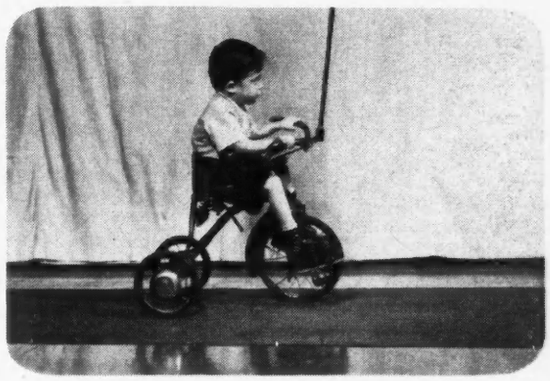
GENERAL

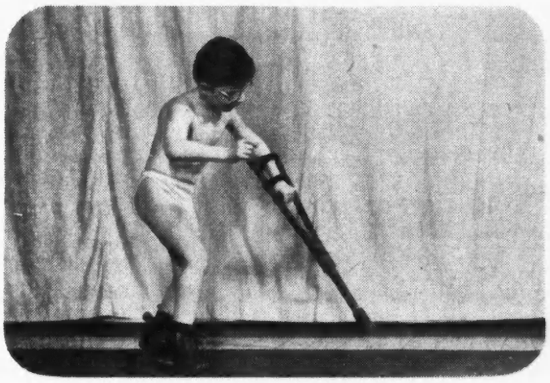
Medical Research Fellowships.—The Medical Fellowship Board of the National Research Council is now accepting applications for the following postdoctoral research fellowships for 1952-1953.

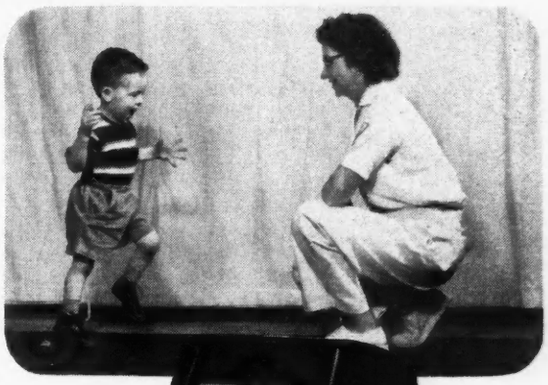
Fellowships in the Medical Sciences.—There are two groups of these fellowships, one supported by The Rockefeller Foundation, and another by The Lilly Research Laboratories. They provide opportunity for training in research in all branches of medical science. The Rockefeller Fellowships are open to citizens of the United States or Canada, the Lilly Fellowships only to citizens of the United States. Fellows must hold the M.D. or Ph.D. degree. The awards are intended for recent graduates who, as a rule, are not more than thirty years of age.

Fellows will be appointed at a meeting of the Medical Fellowship Board early in March, 1952. Applications for consideration at this meeting must be filed on or before December 15, 1951. Appointment may begin at any time determined by the Board. For further information about these fellowships, address the Secretary of the Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, N.W., Washington 25, D.C.

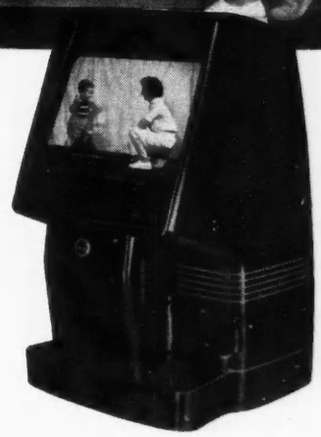








Photographs, courtesy of The Edith Hartwell Clinic of the Strong Memorial Hospital, Le Roy, N.Y.



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The following have been attending postgraduate courses at the Cook County Graduate School of Medicine, Chicago. J. H. A. MacDonald, M.D., Connaught, Ontario; Herbert A. Mosser, M.D., 129 Crawford, Sarnia, Ontario; H. W. Chestnut, M.D., Moosomin, Saskatchewan; B. W. Hargarten, M.D., 403 Carola Bldg., Saskatoon, Saskatchewan; Gordon S. Musick, M.D., Shaunavon, Saskatchewan.

Award for Outstanding Research in the Field of Infertility.—The American Society for the Study of Sterility announces the opening of the 1952 contest for the most outstanding contribution to the subject of infertility and sterility. The winner will receive a cash award of one thousand dollars, and the essay will appear on the program of the 1952 meeting of the Society. Essays submitted in this competition must be received not later than March 1, 1952. For full particulars concerning requirements of this competition, address The American Society for the Study of Sterility, 20 Magnolia Terrace, Springfield, Massachusetts.

The International Hæmophilia Society was formed in 1942. Its object is to assist hæmophiliacs generally and in various ways to promote the study of hæmophilia. The Society depends on voluntary subscriptions and would welcome contributions, as well as correspondence with those interested in its work. The address is The Galton Laboratory, University College, Gower Street, London, W.C.1., England.

Death Rate Drops to Record Low.—A further significant decline in Canada's death rate from tuberculosis is reported in the preliminary figures for 1950 just released by the Dominion Bureau of Statistics. The new figures of 25.9 per 100,000 is a record low and represents a total of 3,582 deaths across the Dominion. These figures are noteworthy in that they include, for the first time, our new province of Newfoundland.

There are several significant features about the new rates. The decline in mortality is general in all provinces except Prince Edward Island which, because of the smallness of its population, frequently shows marked fluctuations. When one considers that the total number of deaths from tuberculosis in P.E.I. during 1950 was only 29, the increase in the death rate from 23.4 to 30.2 assumes its true perspective.

It is noteworthy that the overall rate for Canada has fallen, for the first time in our history, to the twenties. The 1949 figure of 30.4, the previous all-time low, was still hovering above the line. Now we have reached the same decade as the United States which, for 1950, reports a provisional death rate of 22.2 per 100,000.

A further point of interest in respect to this year's statistics is the fact that the greatest reduction has occurred in the provinces which in 1949 had the highest rates. Quebec, British Columbia and New Brunswick, which in 1949 topped the mortality list, have dropped the greatest number of points in 1950.

The honour of having the lowest rate in the Dominion goes again in 1950 to Ontario with the exceptionally low figure of 13.0. This is a record of which to be justly proud. Saskatchewan came next with a rate of 18.5 and the other provinces in order are: Alberta, 19.3; Manitoba, 22.8; Nova Scotia, 26.1; British Columbia, 27.6; Prince Edward Island, 30.2; New Brunswick, 30.5; Quebec, 39.3; and Newfoundland, 68.5.

When one comes to examine the figures from the standpoint of sex and age, it is interesting to note that more men than women died of tuberculosis in Canada during 1950. Out of a total of 3,582 deaths, 2,022 were male and only 1,560 female.

The most vulnerable age groups, on the basis of the 1950 figures, would appear to be young women between 20 and 29 and men between 40 and 69. The number of deaths is also high, however, in women 30 to 39 years and men 20 to 39 years.

New U.S. Figures.—A continued decline in the mortality from tuberculosis is reported in the United States for the year 1950. According to provisional figures released by the National Tuberculosis Association, the death rate has fallen from the 1949 provisional figure of 26.1 to 22.2 per 100,000 in 1950. Medical authorities state that this decline in recent years is "probably due to the increased use of excisional surgery and chemotherapy".—*Bull. Canad. Tuberc. Assoc.*, October, 1951.

Urology Convention-seminar January 7 to 12, 1952 at Montreal. Sponsored by the Northeastern Section of The American Urological Association, and under the Auspices of McGill University and the University of Montreal. The course will be a review of the basic sciences as related to Urology. Considerable time will be devoted to Anatomy, Physiology and Biochemistry. The Pathology and Bacteriology of Urological Diseases will be dealt with in considerable detail. The basic principles of modern urology will be stressed, and all recent advances will be outlined. The faculty has been selected from many universities of both Canada and the United States. Address all communications to the Secretary, Dr. S. A. MacDonald, 1414 Drummond St., Montreal.

BOOK REVIEWS

THE 1950 YEAR BOOK OF DRUG THERAPY

Edited by H. Beckman, Director, Department of Pharmacology, Marquette University School of Medicine. 566 pp., illust. $5.00. The Year Book Publishers Inc., Chicago, 1950.

This book will prove most useful to those who would like to learn about the newer drugs from sources other than the detail man. In summary form it covers the important papers published from October 1949 to September 1950 inclusive; when these are numerous the author discusses the general status in a concise and amusing style. There are sixteen main headings, including allergy, endocrinology, gastroenterology, etc.; it is not surprising that of the book's 530 pages of text some 90 are devoted to the treatment of infectious diseases, mostly with antibiotics, and an equal number to the treatment of cardiovascular diseases; however, in the next edition we shall expect to see more than 200 pages to cover endocrinology, under which heading the greater part of the discussion of ACTH and cortisone is centred.

The introduction is in the form of an excellent review of advances in drug therapy during the period 1940 to 1950, again discussed under headings. This concise summary makes it easy to look up quickly the most recent advances in the treatment of a specific condition, the details of which are found in the later text.

NITROUS OXIDE-OXYGEN ANÆSTHESIA

F. W. Clement, Diplomate American Board of Anæsthesiology; Fellow of International College of Anæsthetists. 369 pp., illust., 3rd ed. $7.80. Lea & Febiger, Philadelphia; Macmillan Company of Canada Ltd., Toronto, 1951.

With the introduction of new drugs and new concepts the field of anæsthesiology has advanced rapidly in the past decade. In keeping with the rapid change Dr. Clement has revised and rewritten his third edition on nitrous oxide-oxygen anæsthesia. Primarily this text discusses the fundamentals of nitrous oxide-oxygen anæsthesia which remain unchanged. For the proper understanding of the fundamentals of nitrous oxide-oxygen anæsthesia the author has considered the physiology of the respiratory and the cardiovascular system, including the close inter-relationship of hypoxia, carbon-dioxide excess, and asphyxia and the clinical significance

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of the carotid and aortic bodies. New stress has been placed on preoperative sedation, which is essential for safe and successful nitrous oxide-oxygen anæsthesia. The introduction of new drugs increased the popularity of this agent. The most important supplementary drug is curare, and a section is devoted to nitrous oxide-oxygen and curare. Throughout the author stresses the essentials for safe administration: the familiarity with the signs of anæsthesia; an open airway; and the maintenance of efficient breathing. The book is a valuable aid for the understanding of nitrous oxide-oxygen anæsthesia especially for individuals in training for anæsthesiology.

DISEASES IN OLD AGE

R. T. Monroe. 407 pp. $8.00. Harvard University Press, Cambridge, 1951; S. J. Reginald Saunders & Co. Ltd., 84-86 Wellington Street, West, Toronto, 1951.

This is a book that can be read with pleasure and profit by any medical man, specialist or not, who has to treat people over sixty years of age. It is a study of 7,491 patients over 61 who were admitted to the Peter Bent Brigham Hospital in Boston over a period of thirty years. The author is now head of a special Department of Geriatrics in this hospital and he has produced a most useful study of his material.

Every page is interesting and many of them are corrective of time honoured ideas. It is impossible to condense this work into a short review or to quarrel with any of the findings presented. It just emphasizes the importance of giving old people a chance to benefit from good medical treatment despite the fact that some of them have lived a very long time. One instance is the attitude toward biliary disease. Patients with gall stones—there were 294 men and 716 women—should have the benefit of surgical treatment unless some factor other than age is a contraindication. Gall stones are not to be trifled with. Mental deterioration seems to be more common in old women than in old men but all cases are helped by intelligent treatment. Many teachers of surgery will be astonished to learn that ten out of sixteen cases of femoral hernia occurred in the male.

The problems of geriatrics are becoming more and more complicated. In 1913, 6.67% of admissions to the Peter Bent Brigham Hospital were 61 years of age. In 1943 this percentage had risen to 20. A similar state of affairs occurs in every other hospital. This book is an essential to practitioners in and out of hospital practice.

THE ENZYMES

Edited by J. B. Sumner, Laboratory of Enzyme Chemistry, Cornell University, Ithaca, N.Y., and K. Myrback, Institute for Organic Chemistry and Biochemistry, University of Stockholm, Sweden. Vol. I, Part 1. 724 pp. illust. $13.50; Vol. I, Part 2. 1361 pp. $12.80. Academic Press Inc., 125 East 23rd Street, New York 10, 1951.

The reactions occurring within living organisms are all catalyzed reactions and most of the catalysts that assist in these reactions are of biological origin. In fact life itself may be considered as a catalyzed process; at least it is a very definitely controlled catalyzed process. This volume, the first of a two-volume series, brings together in a comprehensive survery work done in the enzyme field. It enables one to properly evaluate progress made and also points out the many problems still to be evaluated. The series, when completed, will be in 2 volumes published in 4 parts. The material is prepared by some 87 authorities from Australia, Europe and the United States. Part 1 of Volume 1 begins with an introductory chapter concerning enzymes in general. Chapters 2 to 8 deal with certain chemical and physical aspects of enzymes more or less common to all. Chapters 9 to 19 detail specific enzymes or groups of enzymes. Part 2 of Volume 1 represents a continuation of the study of various specific enzymes or enzyme groups and contains 24 chapters.

Appropriate references are given throughout this volume. The author and subject indexes for both parts of Volume 1 are given in Part 2. There is surprisingly little repetition which might be expected in a volume prepared by so many authors. The reviewer considers this volume a "must" for anyone interested in enzymology, whether in the medical field or in any of the other divisions of the biological sciences, in organic or in physical chemistry.

Books Received

Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Human Biochemistry. I. S. Kleiner, Professor of Biochemistry and Director of the Department of Biochemistry, New York Medical College, Flower and Fifth Avenue Hospitals; formerly Associate, The Rockefeller Institute for Medical Research, New York. 696 pp., illust., 3rd ed. $8.00. The C. V. Mosby Co., St. Louis; McAinsh & Co., Ltd., Toronto, 1951.

Physical Biochemistry. H. H. Bull, Professor of Chemistry, School of Medicine, Northwestern University. 355 pp., illust., 2nd ed. $5.75. John Wiley & Sons, Inc., New York; Chapman & Hall, Ltd., London, 1951.

Studies of Undernutrition. Members of the Department of Experimental Medicine, Cambridge, and Associated Workers. 404 pp., illust. 12s. 6d. net. His Majesty's Stationery Office, 1951.

Medical Dictionary, English-French-German. E. Veillon, formerly Surgeon-in-Chief, Deacon-Hospital, Riehen-Basel, Switzerland. 1407 pp. Grune & Stratton, New York; The Ryerson Press, Toronto, 1951.

Technical Methods for the Technician. A. L. Brown. 784 pp., illust., 4th ed. $10.00. Anson L. Brown Inc., Columbus, Ohio, 1950-51.

Surgery of the Stomach and Duodenum. C. E. Welch, Associate Visiting Surgeon, Massachisetts General Hospital; Clinical Associate in Surgery, Harvard Medical School. 349 pp., illust. $8.50. The Year Book Publishers, Inc., Chicago, 1951.

Diabetes Control. E. L. Bortz, Chief of Medical Service B. The Lankenau Hospital; Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 264 pp., illust. $4.20. Lea & Febiger, Philadelphia; Macmillan Co. of Canada Ltd., Toronto, 1951.

The Versatile Victorian. Z. Cope. 179 pp. $3.00. Harvey & Blythe Ltd., London; The Copp Clark Co. Ltd., Toronto, 1951.

Syphilis. R. S. Weiss, Professor Emeritus of Clinical Dermatology, School of Medicine, Washington University; and H. L. Joseph, Consultant in Dermatology and Syphilology, U.S. Air Force Base. Travis Air Force Base, California. 180 pp., illust. $5.00. Thomas Nelson & Sons, New York, Edinburgh, Toronto, 1951.

Headache. L. G. Moench, Assistant Clinical Professor of Medicine, University of Utah School of Medicine. 217 pp., illust., 2nd ed. $4.50. The Year Book Publishers Inc., Chicago, 1951.

New and Nonofficial Remedies, 1951. The Council on Pharmacy and Chemistry, American Medical Association. 782 pp. $3.75. J. B. Lippincott Co., Philadelphia, London and Montreal, 1951.

Anatomy in Surgery. P. Thorek, Assistant Clinical Professor of Surgery (formerly assigned to Gross and Topographic Anatomy) University of Illinois College of Medicine; Diplomate of the American Board of Surgery: Associate Professor of Topographic Anatomy and Clinical Surgery, Cook County Graduate School of Medicine. 970 pp., illust. $25.00. J. B. Lippincott Co., Philadelphia, London and Montreal, 1951.

Management of Cœliac Disease. S. V. Haas, Professor of Pædiatrics and Director of the Department, New York Polyclinic Medical School and Hospital, and M. P. Haas. 188 pp. $5.00. J. B. Lippincott Co., Philadelphia, London and Montreal, 1951.

Global Epidemiology. J. S. Simmons, Brigadier General, United States Army, Retired, Dean and Professor of Public Health, Harvard University School of Public Health. T. F. Whayne, Colonel, M.C. United States Army, Chief, Preventive Medicine Div. Office of the Surgeon General, United States Army. G. W. Anderson, Mayo Professor and Director, School of Public Health, University of Minnesota. H. M. Horack, Member of Staff, Dept. of Medicine and Section of Cardiology, Ochsner Clinic, New Orleans. 652 pp., illust. Volume 2. $17.00. J. B. Lippincott Co., Philadelphia, London and Montreal, 1951.

Open-chain Ureide Sedatives—An Objective Review. F. G. Hobart, Ph.C., Member of the Pharmaceutical Society, formerly Lecturer on the Chemistry and Pharmacology of Anæsthetics and Related Drugs to the Fellowship of Postgraduate Medicine, etc. 27 pp. Leonard Hill Ltd., London, 1951.

Food and You. E. S. Nasset, Professor of Physiology, Department of Physiology and Vital Economics, School of Medicine and Dentistry, University of Rochester, Rochester, New York. 92 pp. $3.50. Charles C. Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1951.

The Physiology of the Newborn Infant. C. A. Smith, Associate Professor of Pædiatrics, Boston Lying-in Hospital, Harvard Medical School. 348 pp., illust., 2nd ed. Charles C. Thomas, Springfield; The Ryerson Press, Toronto, 1951.

The Pharmacologic Principles of Medical Practice. J. C. Krantz, Jr., Professor of Pharmacology, School of Medicine, University of Maryland. 1116 pp., illust., 2nd ed. $11.25. Burns & MacEachern, Toronto, 1951.

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POSITION VACANT.—Resident physician for 150-bed hospital. Contagious diseases and tuberculosis in children. $125.00 per month. Apply The Medical Superintendent, Alexandra Hospital, 230 Charron Street, Montreal.

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